MORBIDITY ASSOCIATED WITH WORKING IN OPERATING THEATRES

ALASTAIR ANDREW SPENCE

M.B., Ch.B., F.F.A.R.C.S.

Thesis submitted for the degree of

Doctor of Medicine

University of Glasgow

University Department of Anaesthesia

Western Infirmary, Glasgow.

November 1975.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

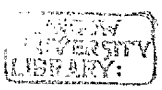


TABLE OF CONTENTS

	Page
List of tables	2
List of illustrations	4
Statement of Collaboration	5
Acknowledgements	6
Statistical Analysis	7
Summary	8
Chapter 1 Background to the Problem	
The Problem of Operating Theatre Contamination	11
Patterns of contamination	12
The Effects of Anaesthesia on Cell Division ...	13
Teratogenicity	14
The Metabolism of Anaesthetics	16
Anaesthesia and the Pregnant Woman	16
Early Surveys of Obstetric History	17
Other Possible Toxic Effects	23
Mortality Surveys	23
Cancer	24
Hepatitis	25
Conclusions	26
Chapter 2 The First U.K. Survey	
General Considerations and Objectives	28
The Questionnaires	29
The Cohorts (a) Anaesthetists	30
(b) Controls	31
Handling of the Questionnaires	32
Replies	33
Analysis of Replies	35
Discussion: Reply Rate	52

Page

Discussion: Abortion 52

Congenital Abnormality 53

Infertility 54

Design of the Questionnaire 55

Analysis of Replies from Women Aged 25-35 Years 55

Conclusions 56

Suggested Further Action 57

General Attitudes to These Data ... 58

Chapter 3 The Second United Kingdom Survey: Male Doctors

Purpose 59

Method 59

The Questionnaire 60

Analysis of Data 61

Response 62

Results: Abortion 62

Congenital Abnormality 67

Stillbirth and Death 70

Infertility 70

Matched Data 70

Discussion: Abortion 74

Congenital Abnormality 77

Matched Data 78

Chapter 4 Second U.K. Survey: Illness in Male Respondents

Introduction 82

Results: 82

Liver Disease 84

Kidney Disease 89

Diseases of Bones and Joints 89

Cardiovascular Disease 89

Gastrointestinal Disease 94

Page

Discussion 94

Chapter 5 Comparison of U.K. and U.S. Data

The Three Surveys 102

Female Surveys 103

Male Surveys 103

Results: Female Respondents 106

Spontaneous Abortion 106

Congenital Abnormalities 108

Male Respondents 108

Spontaneous Abortion 110

Congenital Abnormalities 110

Other Diseases 111

Discussion 113

Chapter 6 Conclusions, Recommendations and Further Investigation

Health Hazards 115

Operating Theatre Contamination 115

Future Action 116

Plan of Investigation:

Controlled Prospective 5 Year Survey of Women Anaesthetists 117

Advice to Theatre Staff 119

References 120

Appendix A Female Survey Questionnaire (Anaesthetist)

" B " " " (Control)

" C " " " Explanatory Letter

" D " " " " "

" E Follow-up letter

" F Male Survey Questionnaire

" G Explanatory Letter

" H Follow-up Letter

" I U.S. Questionnaire

LIST OF TABLES

Table 1	Summary of findings in the Copenhagen study (Askrog and Harvald, 1970).
Table 2	Data from Cohen, Bellville and Brown (1971).
Table 3	Female survey. Details of questionnaires sent, and computation of reply rate.
Table 4	Numbers married in the two groups, and mean ages.
Table 5	Pregnancies, sex of children, stillbirths and neonatal deaths.
Table 6	Spontaneous abortion.
Table 7	Number having one and more than one abortion.
Table 8	Congenital abnormality of liveborn children.
Table 9	Congenital abnormality with reference to the function or anatomical system involved.
Table 10	Involuntary infertility.
Table 11	Pregnancy after infertility.
Table 12	Respondents 25 - 35 years old (inclusive) at the time of survey. General data.
Table 13	25 - 35 yrs inclusive. Pregnancies, abortion and congenital abnormality.
Table 14	Involuntary infertility in 25-35 yr group.
Table 15	Full-time and part-time appointments. Comparison of data.
Table 16	Survey of male doctors : mailing data and reply rates.
Table 17	Male survey : comparison of replies to 1st and 2nd mailings.
Table 18	Male survey : spontaneous abortion.
Table 19	Male survey : analysis of 1st and 2nd pregnancies.
Table 20	Male survey : congenital abnormality.
Table 21	Types of congenital abnormality.
Table 22	Survey of male anaesthetists. Retrospective matching of data: male exposure.

Table 23 Male survey. Retrospective matching of data: female exposure.

Table 24 Male survey. Retrospective matching of data: female exposure.

Table 25 Male survey. Retrospective matching of data: female exposure.

Table 26 Female exposure. Comparison of data from U.K. female anaesthetists study and data of exposed females obtained in the course of the U.K. male study.

Table 27 Infertility. Comparison of data from the two U.K. surveys.

Table 28 Male survey. Age and % reporting ill.

Table 29 Multiple disease reporting and specialty.

Table 30 Reported disease rates.

Table 31 Liver diseases

Table 32 Hepatitis

Table 33 Joint disease

Table 34 Lumbar or cervical disc and associated problems.

Table 35 Cardiovascular disease.

Table 36 Cardiovascular disease and speciality.

Table 37 Angina, infarctions, hypertensions and arrhythmias.

Table 38 Gastrointestinal disease.

Table 39 Gastrointestinal disease in three occupational groups.

Table 40 Combined analysis : total mailings and replies.

Table 41 Adjusted data from combined surveys of female physicians in the U.K. and U.S.

Table 42 Adjusted data from combined surveys of male physicians in the U.S. and U.K.

Table 43 Disease rates per 100 for male anaesthetists and non-anaesthetist controls in the U.K. and U.S.

LIST OF ILLUSTRATIONS

Fig 1. Abortions per cent plotted against week of gestation.

Fig 2. Distribution of hepatitis in three work categories. Respondents older and younger than 47 years.

STATEMENT OF COLLABORATION

Dr. R.P. Knill-Jones, formerly of the Department of Medicine in Relation to Mathematics and Computing, and now of the Hospital Health Services Research Unit (Western Infirmary), University of Glasgow, has been a co-worker throughout these studies. He and the author undertook the data analysis jointly although Dr. Knill-Jones was responsible entirely for writing the computer programs used in the analysis.

The author was the instigator of the various studies, designed the draft questionnaires, and was responsible for the preparation, despatch, receipt and editing of the questionnaires. In these aspects of the work, he received help from Dr. Lucia V. Rodrigues, Registrar in Anaesthetics, Western Infirmary, and Dr. D.D. Moir, Consultant Anaesthetist, Queen Mother Hospital, in the first study (Chapter 2) and Dr. B. Joyce Newman, Senior Registrar in Anaesthetics, Western Infirmary in the second study (Chapters 3 and 4).

The author had no part in the collection of the U.S. data used in the combined analysis (Chapter 5). The U.S. - U.K. collaborative exercise was undertaken jointly by the author and Professor E.N. Cohen, University of Stanford, California, who were joined by Dr. Knill-Jones, Glasgow, and Dr. Byron W. Brown, Department of Community and Preventive Medicine, Stanford.

Publications: (Authors' names in alphabetical order. Manuscripts prepared by A.A.S.)

Knill-Jones, R.P., Moir, D.D., Rodrigues, L.V. and Spence, A.A. (1972) Anaesthetic Practice and Pregnancy. Controlled survey of women anaesthetists in the United Kingdom. The Lancet, 1, 1326.

Knill-Jones, R.P., Newman, B.J. and Spence, A.A. (1975) Anaesthetic Practice and Pregnancy. Controlled survey of male anaesthetists in the United Kingdom. The Lancet, 2, 807.

ACKNOWLEDGEMENTS

I wish to acknowledge the following, in addition to those colleagues whose names appear in the Statement of Collaboration.

My secretaries Mrs. M. MacLeod and Mrs. M. Smith.

The University of Glasgow, the Board of Management for Glasgow Western and Gartnavel Hospitals and Imperial Chemical Industries Limited who provided financial assistance.

Dr. V.M. Hawthorne and Dr. Gerald Richards,* University of Glasgow, and Professor Martin Vessey, University of Oxford, who gave valuable advice on the analysis and interpretation of the data.

The various offices of the University Court who assisted in facilitating the despatch of the questionnaires and the reply-paid system.

The Department of Health and Social Security (particularly Mr. Lucas) and the Scottish Home and Health Department (particularly Mr. Stevenson) for allowing me access to their records.

The Association of Anaesthetists of Great Britain and Ireland. The Faculty of Anaesthetists, Royal College of Surgeons of England, and the secretaries of the various regional anaesthetic societies.

My clinical and technician colleagues who, at various times, cheerfully lent a hand in filling and sealing many thousands of envelopes.

* Now at the University of Leeds.

STATISTICAL ANALYSIS

Unless stated otherwise, the chi-squared test (X^2) has been used to test the significance of differences in frequencies between groups.

Where 2 x 2 contingency tables could be constructed, the Yates' modified X^2 test (1934) has been applied.

In the situation of ($N<50$) Fisher's Exact Test has been employed. This is indicated clearly in either the text or the tables, or both.

In general, a probability value (P) of less than 5% has been the criterion of statistical significance.

The author has relied heavily on Langley, R. (1970) "Practical Statistics" London : Pan Books.

MORBIDITY ASSOCIATED WITH WORKING IN OPERATING THEATRES

ALASTAIR ANDREW SPENCE, MB ChB FFARCS

SUMMARY

Operating theatre air becomes contaminated with gaseous anaesthetics and these are taken up by the blood and other tissues of theatre personnel. The fact that the general anaesthetics, in concentrations which produce anaesthesia, exhibit a wide variety of actions on cell mechanisms and tissue growth, including teratogenicity and carcinogenesis, has caused speculation about possible health hazards from the much smaller concentrations to which theatre workers are exposed.

This thesis describes two controlled surveys of anaesthetists in the United Kingdom. In the first, 563 married women anaesthetists were compared with 828 married women doctors who were not anaesthetists. Anaesthetists who worked during a pregnancy had an increased frequency of spontaneous abortion compared with the controls whose frequency was similar to that of a small group of non-working anaesthetists. Working anaesthetists had an increased frequency of congenital abnormality of liveborn children and the women anaesthetists, as a group, had a frequency of involuntary infertility twice that of the controls.

The triad of abortion, congenital abnormality and infertility might suggest an abnormality of foetal development, perhaps as a consequence of drug toxicity. However, factors such as the pattern of abnormalities and the maturity of the abortions cast doubt on this hypothesis.

In the second survey, questionnaires were mailed to all the male /...

anaesthetists in the U.K. and an appropriate number of control doctors. 70.0% replied. There was no obvious effect on obstetric history of the marriages where the father had worked in an operating theatre (exposed). Although paternal exposure was not associated with an increase in the major congenital abnormalities, anaesthetists reported a higher proportion of minor abnormalities.

However, there is reason to believe that anaesthetists are more likely to report such problems. Male anaesthetists did not appear to be less fertile than the controls.

In this second survey, there were 523 pregnancies in which maternal exposure had occurred. In this group, the frequency of spontaneous abortion was 40% greater than in the controls and, while the numbers were too small to allow a confident estimate, the proportion of congenital abnormalities was increased.

Retrospective matching (maternal exposure versus no exposure) with respect to maternal age, parity and smoking confirms the increased risk of abortion associated with maternal exposure which is estimated to be in the range 158 - 271%.

Replies about the general health of the male respondents suggest that anaesthetists have an increased incidence of hepatitis and disorders of the lumbar spine and there is uncertainty about their susceptibility to peptic ulceration and arterial hypertension. Male anaesthetists do not appear to be specially susceptible to cancer or renal disease.

These data have been re-examined in collaboration with a team which has conducted a similar enquiry in the United States. There is close agreement between the two countries regarding female exposure and /...

abortion although the evidence concerning congenital abnormality is stronger in the U.S. than in the U.K. The increased risk of hepatitis in male anaesthetists has been confirmed, as have the U.K. data on cancer and renal disease.

These findings have prompted measures to reduce operating theatre air contamination. Although such precautions are sensible, no direct link exists between morbidity in anaesthetists and theatre contamination. To assume otherwise is undesirable and prospective monitoring of the health of theatre personnel is essential.

CHAPTER 1 BACKGROUND TO THE PROBLEM

The Problem of Operating Theatre Contamination

From the earliest days of inhalation anaesthesia, it has been the practice to allow the patient's expired gas to be discharged into the immediate environment. The earliest manifestation of concern about this was the installation of anti-static precautions and other measures to prevent an explosion in environments contaminated with substances such as diethyl ether and cyclopropane.

Hewer (1972) implies that the problem of theatre air contamination was at its worst when open systems were employed and he describes how the family of an anaesthetist might complain of smelling the anaesthetics from the anaesthetist's own expired gas even after he had returned home in the evening. However, such complaints occur at the present time and, in the last 25 to 30 years, the large increase in the frequency of surgical operations, long operating lists, and a more leisurely approach to surgery resulting in longer operating times have caused anaesthetists and other operating theatre workers to spend most of the working day in the operating theatre, - almost certainly a greater number of hours per week than their predecessors.

The development of modern techniques, particularly in the U.K. where circle absorber systems (closed or semi-closed) have been unpopular, have resulted in the discharge of volumes of contaminated gases equal to or greater than the patient's minute volume. For example, a recent enquiry by the author as to the practice of ten Consultant Anaesthetists in different teaching hospitals revealed that they exceed the recommended fresh gas flow rates for a Magill circuit by a factor of 2 (10 litre/minute).

At various times, reports have appeared or statements have been made to suggest that the practice of anaesthesia may be associated with specific risks to health. Some of these are reviewed in this chapter. The thesis reports findings of two large surveys in the United Kingdom with special reference to the obstetric history of women working in anaesthesia. Although specific patterns of morbidity appear to exist, no direct connection has been shown. Nevertheless, the data contained in this thesis will be regarded by many as circumstantial evidence of a harmful effect of operating theatre contamination by anaesthetic gases. Thus, pollution of operating theatres is a continuing secondary theme of this communication.

Patterns of Contamination

Measurement of contaminants in operating theatre air was facilitated by the development, particularly in the 1960s, of sophisticated detector systems for use in conjunction with a gas chromatograph, for example flame ionisation detectors and electron-capture detectors. Developments in mass spectrometry have allowed an alternative approach to the problem, although all the major reports of pollution measurements so far are the result of gas chromatographic techniques. Concentrations of contaminants depend on the quantities discharged from the patient's circuit, the size of the operating theatre and the efficiency of the theatre air ventilating system. Even when these factors are allowed for, there may be considerable variation within the operating theatre, but it is generally agreed (Corbett and Ball, 1971) that the highest concentrations occur in the region immediately around the head of the patient. Traditionally, it is at this point that the anaesthetist positions himself, although others who may share this zone, for example ear, nose and throat surgeons and dentists, may be exposed to equally high concentrations. Examination of the literature on this subject suggests that typical values of contamination are /...

15p.p.m. for halothane and 600-700p.p.m. for nitrous oxide (Linde and Bruce, 1969; Askrog and Petersen, 1970; Hallen, Ehrner-Samuel and Thomason, 1970; Whitcher, Cohen and Trudell, 1971). The concentration in the region of the anaesthetist may be 10 times that of the average value (Corbett and Ball, 1971) although the institution of appropriate scavenging systems may reduce the level of contamination by a factor of 10 (Whitcher, Cohen and Trudell, 1971).

Patients in whom the administration of anaesthesia has ended continue to be a source of contamination and Pfaffli and others (1972) have shown there are measurable quantities of halothane and nitrous oxide in the air of recovery rooms in which patients who have received these agents are nursed.

In addition to the detection of gaseous anaesthetics in operating theatre air, Whitcher, Cohen and Trudell (1971) have shown that the concentrations present in the expired gas of the anaesthetist support the assumption that those who work in contaminated environments reach equilibrium with the concentrations of the contaminants. The present views on the pharmacokinetics of the inhalational anaesthetics would suggest that the clearance of agents from the tissues of such exposed persons would be a relatively rapid process, particularly in the case of a relatively insolluble anaesthetic such as nitrous oxide (Eger, 1971). However, Corbett and Ball (1971) have shown that detectable concentrations of nitrous oxide and halothane are present in the expired gas of an anaesthetist as long as 6 and 64 hours respectively after he has left the operating theatre environment.

The Effects of Anaesthesia on Cell Division

A wide variety of studies of circumstances in which cell division can be observed show that most, if not all, of the gaseous anaesthetics/...

interfere with cell division by prolonging the period of D.N.A. synthesis (Stage of the Interphase of cell division) although their effect is most obvious as an inhibitor of mitosis (Fink, 1971). The theory has been advanced that anaesthetics stimulate the formation of chalones, substances which inhibit mitosis, and it can be demonstrated that anaesthetics inhibit spindle formation in the cell.

Andersen (1966) demonstrated depression of cell division by general anaesthetics and emphasised the role of spindle inhibition, causing an interruption of the transition from prophase to metaphase. The removal of the anaesthetic allows the mitotic process to continue (Rao, 1968). It should be noted, however, that the concentrations at which these effects have been studied are of a similar order to those required for general anaesthesia of an animal or man; that is close to the MAC value, or a multiple of MAC value.

In many studies, it has been demonstrated that anaesthetics inhibit growth of a wide range of creatures and processes: chick embryo (Kieler, 1957); fungi (Schreiner and Gregoire, 1963); protozoon (Nunn, Dixon and Moore, 1968); carnations (Crocker and Knight, 1908); leucocytes (Aldrete and Virtue, 1967; Eastwood et al, 1963); fibrosarcoma transplants in mice (Fink, 1966); DNA synthesis (Bruce and Taurig, 1969). The depression of the white cell count in man as a result of exposure to nitrous oxide is well known (Lassen et al, 1956; Parbrook, 1969).

Teratogenicity

The dividing cells in the embryo are susceptible to drugs and other cytotoxins as are the dividing cells in other growing tissues, although the outward manifestation of the injury is different (Fink, 1971). The teratogenicity of anaesthetics has been demonstrated clearly in other /...

species (Smith, Gaub and Moya, 1965; Fink, Shephard and Blandau, 1967; Basford and Fink, 1968; Smith, Gaub and Learer, 1968; Snegireff, Cox and Eastwood, 1968). Although it is recognised that there is considerable interspecies variation in the teratogenicity of drugs, studies in the rat show that exposure to nitrous oxide at about half the concentration necessary to produce anaesthesia causes a high incidence of supernumerary lumbar ribs and delayed appearance and fusion of the vertebral centres at the thoraco lumbar junction. Prolonged exposure to nitrous oxide causes a marked selective destruction of the male foetus in rats, although there is a high death rate in foetuses of both sexes. Fluorinated hydrocarbons cause a high death rate in chick embryos while cyclopropane is "frankly" teratogenic (Andersen, 1968). Andersen found two effects on mitosis in the neural tube of the embryo: (1) at low concentrations of cyclopropane, there was an arrest of metaphase manifested as an increase of the mitotic index; (2) there was a decrease in cells entering mitosis at both low and high concentrations of cyclopropane. He found that exposure to the anaesthetic for more than 3 hours was necessary to induce the changes but that some embryos were capable of recovering after the anaesthetic had been withdrawn for about 24 hours.

All the studies of teratogenicity and foetal death reported above relate to concentrations of anaesthetics close to those used for clinical anaesthesia. However, these studies have stimulated interest in the possibility that tissue concentrations at a substantially lower level, such as might occur as a result of exposure to the operating room environment might also be associated with teratogenicity. Corbett and others, (1973), have demonstrated an increased foetal death rate in rats exposed to low concentrations of anaesthetics during the early phase of the pregnancy (6 - 10 days). The concentrations of nitrous oxide were in the range 1,000 to 10,000 p.p.m. Bruce (1973) was unable to produce /...

a similar effect in rats exposed to trace concentrations of halothane and the same author has been unable to confirm the studies of Corbett using nitrous oxide (Bruce, personal communication). Corbett (personal communication) has been unable to demonstrate an effect on the rat foetus from trace concentrations of methoxyflurane. At the time of writing, studies of a similar nature are being continued in both the United States and the United Kingdom.

The Metabolism of Anaesthetics

In spite of earlier views that many of the gaseous anaesthetics behaved in the body as inert substances, there is increasing evidence that small quantities of the inhalation anaesthetics are metabolised in man (Van Dyke and Chenoweth, 1965; Cohen, 1971) although, apart from the nephrotoxicity of methoxyflurane (Mazze, 1971), the implications of metabolism for tissue toxicity are not known. Cascorbi, Blake and Helrich (1970) were unable to show convincing evidence that halothane causes enzyme induction, although enzyme induction by the inhalational anaesthetics has been demonstrated in animals (Van Dyke, 1966; Linde and Berman, 1971).

Anaesthesia and the Pregnant Woman

The thalidomide disaster of the late 1950s stimulated enquiry about the possible teratogenic effects of anaesthetics in man. The only systematic enquiry in humans was that of Shnider and Webster (1965) whose data, although to be regarded only as a pilot study, suggested that women who are in the early stages of pregnancy and who are exposed to general anaesthesia were subject to an increased risk of abnormality of the foetus. Although the evidence is far from clear, it is now an accepted practice in most countries of the Western world that anaesthetics/...

shall not be given to a woman in the first trimester of pregnancy unless she requires surgery of an emergency nature. Strunin and others, 1975, have suggested that about 30% of a general surgical female population in the age range 14 - 45 years may be at risk and that, of these, about 60% are likely to be undergoing surgery of a minor nature. This implies that, notwithstanding the accepted practice, there are many women in whom the pregnancy may not be manifest at the time of coming to surgery although regrettably little is known about the outcome of such pregnancies.

Early Surveys of Obstetric History

Vaisman (1967) was the first to publish data which suggested that the practice of anaesthesia by pregnant women might be associated with obstetric complications. His concern was with the general working conditions of anaesthetists in the USSR and he collected, in an uncontrolled fashion, data from 354 anaesthetists, representing more than 15% of those practising anaesthesia in the USSR. His information related principally to subjective experiences such as headache, irritability, fatigue, insomnia, etc. However, he noted without comment that he received information relating to the course and outcome of pregnancy in 31 female anaesthetists aged from 24 to 38 years. 18 pregnancies had terminated in spontaneous abortion and in one subject there had been three abortions. There were two premature births and one infant had congenital deformities. Most of the women had experienced various other disorders during the pregnancy, 13 suffered toxaemia while an unspecified number had "threatened asphyxiation of the foetus" and "hypersensitivity to ether, etc.". Two of the 31 women had discontinued work in the operating theatre because they feared that this was aggravating the risk of abortion and in both of them the pregnancy proceeded to term satisfactorily. Only 17 pregnancies out of an unspecified number were completely free of trouble. All except four of the women who had spontaneous abortions had been working with semi-open/...

circuits, usually with ether and in the absence of any ventilation in the operating theatre. The average duration of anaesthetic practice per week was 25 hours or more, in the women who experienced complications, but the average for the 7 who had no problems was 15 hours.

Although we depend on translations to understand the Vaisman paper, there is little doubt that it is not presented as a serious scientific communication but rather as a propaganda statement. As such, it may have been highly successful since we understand that doctors who practice anaesthesia in the USSR receive an increased remuneration as an acknowledgement of the hazards to which they are exposed. Nevertheless, it would not have been surprising if Vaisman's report, particularly in relation to obstetric complications, had received no lasting attention. However, the matter of obstetric complications was pursued by Askrog and Harvald (1971) in Denmark. They surveyed 752 women, the majority of whom were the wives of male anaesthetists, (these women having not worked in operating theatres themselves) but the survey was extended also to the very small number of women physician anaesthetists in Denmark and to the rather larger number of nurse anaesthetists. A summary of the findings is shown in Table 1 which compares obstetric history before and after commencing employment in anaesthesia. There is an increase in the frequency of spontaneous abortion (abortion/total pregnancies %) apparently associated with commencing employment in anaesthesia, although only in the case of the wives of male anaesthetists does this increase reach the level of statistical significance. The obvious short-coming of such an analysis is that it takes no account of the effect of aging or parity on the frequency of spontaneous abortion and it is not possible to state that these increases were not attributable to these factors entirely. Nevertheless, the authors claimed that the increased frequency of spontaneous abortion associated with employment in anaesthesia might be a result of foetal abnormality as a result of exposure of the germ cells to trace concentrations of volatile anaesthetics.

TABLE 1 Summary of findings in the Copenhagen study (Askrog and Harvald, 1970). Comparison of obstetric history of female anaesthetists, nurse anaesthetists and the wives of male anaesthetists before and after commencing employment in anaesthesia.

	Before Employment	After Employment
Anaesthetists and Nurses:		
Total pregnancies	93	255
Abortions	10 (10.7%)	45 (17.6%)
Liveborn - Male	50 (60.2%)	98 (48.3%)
- Female	33	105
Congenital Abnormality	-	1
Wives:		
Total pregnancies	119	137
Abortions	9 (7.6%) *	28 (20.4%) *
Liveborn - Male	55 (56.1%)	49 (44.5%)
- Female	53	61
Congenital Abnormality	1	3

* $P < 0.05$

The authors drew attention also to the apparent increase in the number of congenital abnormalities following employment in anaesthesia but, perhaps sensibly, they did not dwell in this point in detail since the numbers are unacceptably small. They gave greater emphasis, however, to their observation that the overall sex ratio of the liveborn children appear to have been disturbed as a result of employment in anaesthesia. Thus, anaesthetists appear to produce more female children than male children. It was proposed that this was a result of a specific toxic action on the sperm cells, - it was claimed, without supporting statements, that the double-X (female) cell is better able to withstand such effects.

Cohen, Bellville and Brown (1971), concerned about the demonstrable teratogenicity of anaesthetics in other species, the presumed risk to the pregnant woman undergoing general anaesthesia (Shnider and Webster, 1965), and the demonstration of trace quantities of anaesthetic agents in the blood and expired gas of women in operating theatres, conducted a survey by means of personal interviews of 159 married women nurses in the age range 25-50 years employed in three large general hospitals in Northern California. There were 67 who worked predominantly in the operating room and 92 who worked in general duties outside the operating theatre. A second group of 131 women physicians in the same age range included 50 anaesthetists and 81 physicians. The mean age of the operating theatre ("exposed") groups and the non-exposed groups (controls) were comparable although the physicians tended to be older than the nurses. The obstetric history of these women in the course of the previous 5 years was documented with great care. The principal findings are shown in Table 2. The most striking difference was the large increase in the frequency of spontaneous abortion in the 2 anaesthetic groups. Both differences are statistically significant: nurses $P = 0.045$ (Fisher's exact test), physicians $P = 0.0035$. Both anaesthetist groups had a shorter mean maturity of the aborted foetus. Detailed information on the health and development of the surviving /...

TABLE 2 Data from Cohen, Bellville and Brown (1971) showing differences in obstetric history between women working in anaesthesia and paediatrics (non anaesthetists)

	Anaesthetists	Non-Anaesthetists
Nurses:		
Living children	26	31
Abortions	10	3
Abortions/Pregnancies %	29.7	8.6
Mean Maturity of Abortion (weeks)	8.3	10.0
Physicians:		
Living children	23	52
Abortions	14	6
Abortions/Pregnancies %	37.8	10.3
Mean maturity of abortion (weeks)	7.5	9.5

children of the four groups showed that there was no difference in the levels of physical performance, mental acuity, or in the incidence of congenital defects although the authors appreciated that differences between the groups would be unlikely in a study of relatively small numbers.

These authors concluded that although there may have been other factors to account for the clear difference in the frequency of spontaneous miscarriage, the most obvious difference between the groups was that the anaesthetists were subject to prolonged periods of work in the operating theatre. They drew attention to the possibility that the abortion data might be explained on the basis of operating theatre pollution. They considered that the difference in maturity of the aborted foetus between the exposed and non exposed groups would be in keeping with a hypothesis of drug induced foetal death. It was appreciated that this study could be regarded only as a pilot project and the authors advocated expansion of the study to include larger numbers, cytogenetic examination of the abortuses, parallel experimental studies in other species, and steps to prevent the contamination of operating theatres with anaesthetics.

Although there had been no co-ordination or even mutual awareness of activities on either side of the Atlantic, the nation-wide enquiry in the United Kingdom reported in Chapter 2 was already in progress at the time of the report of Cohen, Bellville and Brown (1971). The relatively uncontrolled observations of Vaisman, and Askrog and Harvald had received considerable (perhaps excessive) publicity at the 3rd European Congress of Anaesthesiology in Prague in September 1970. The most sensational aspects of these reports had been transmitted to both the medical and lay news media and within a short period of time grossly distorted accounts of what had been written were being circulated widely.

Further discussion of these health problems occurs in subsequent chapters of this thesis.

Other Possible Toxic Effects

Although Vaisman (1967) concentrated on the unpleasant aspects of work as an anaesthetist, he did not dwell on operating theatre pollution as the principal factor responsible for the various ills. Nevertheless, he gave a long list of problems to which Russian anaesthetists appear to be particularly prone: headache, irritability, fatigue, insomina, impaired resistance to alcohol, skin irritation, nausea, indigestion, coagulation impairment, bruising and jaundice. Other factors such as prolonged working hours and excessive work-loads were mentioned although it is difficult to see an obvious connection between these and such a wide variety of morbidity. Smith (1975) points out that if there are occupational health hazards in the practice of anaesthesia, there may be many factors which inter-react. It can be shown that trace concentrations of anaesthetics impair mental performance (Salvini, Binaschi and Riva, 1971; Bruce, Bach and Arbit, 1974) although Smith, G. and Shirley, A. in this department have been unable to confirm the findings of Bruce, Bach and Arbit (1974) in spite of employing a similar method of assessment and Williams (1974) cited by Smith (1975) have detected behavioural changes in rats exposed to 1000 and 100 p.p.m. of trichloroethylene.

Mortality Surveys

Bruce and others (1968) conducted a 20 year retrospective survey of the causes of death among members of the American Society of Anesthesiologists comparing them with the fate of clients of the Metropolitan Life Assurance Company. Although there were no significant differences in the frequency of any particular disease, death from malignancy of the /...

lymphoid and reticulo-endothelial systems and from suicide were relatively common among anaesthetists and the rate for lung cancer and coronary artery disease in anaesthetists was less than that in the control group. However, a similar comparison based on 5 years prospective data collection, yielding 211 deaths in anaesthetists which were compared with the previous data from the Metropolitan Life Assurance Company, failed to confirm the trends in the earlier analysis. Happily, a conclusion from both studies was that the overall death rate among American anaesthetists, during their working life, is low by comparison with that of the controls although they hold this to be a finding consistent with what is to be expected in those of a higher socio-economic status. The claim of the authors in the second study (Bruce et al, 1974) that the failure to confirm an increased incidence of lymphoid and reticulo-endothelial tumours is a result of advances in therapy seems fanciful and it is more reasonable to conclude that no special patterns of mortality have been shown in anaesthetists. The possibility of an increase in the frequency of suicide is not peculiar to anaesthetists although it may be a general problem of medical practitioners (Rose and Rosow, 1973).

Cancer

In pursuit of the suggestion of Bruce and others (1968) that cancer may be more prevalent among those who are employed in anaesthesia, Corbett and others (1973) conducted a survey of 621 female nurse anaesthetists in Michigan. An 84.5% reply rate revealed a total of 33 malignancies in 31 nurse anaesthetists. Not surprisingly, a high proportion of these tumours had been diagnosed relatively recently in relation to the time of the survey. Based on the statistics from the Connecticut Tumor Registry, the Michigan nurse anaesthetists appear to be more than 3 times more susceptible than the general population to the development of malignant tumours. The American Society of Anesthetists' Ad Hoc Committee on the Effect of Trace /...

Anaesthetics on the Health of Operating Room Personnel (Cohen and others, 1974) found an increased frequency of cancer among physicians and nurses working in operating theatres in the United States compared with physician and nurse paediatricians, although there was no increase in the incidence of cancer in a controlled comparison of the women members of the Associationsof Operating Room Nurses and of Operating Room Technicians. In the same study, a comparison of males working in operating theatres and males working in paediatrics or general nursing duties did not show any difference between the groups in respect of cancer rates.

Patients with cancer may have an exacerbation of their disease as a result of anaesthesia and operation and it is considered likely that the operative stress alters the resistance to the tumour (Buinauskas, McDonald and Cole, 1958). This may be a result of failure of the immune response (Bruce and Wingard, 1971) which is considered by some to be important in the resistance of the organism against malignancy (Gatti and Good, 1970).

Gaylord and Simpson (1916) inoculated mice with cancer and observed that daily exposure to chloroform or ether anaesthesia for 10 successive days appeared to stimulate tumour growth and subsequent reports have tended to support the concept that anaesthetic agents may promote the development of cancer (Trevino and Gines, 1961; Agostino and Cliffton, 1964) although different reports deny such an effect (Schatten and Kramer, 1958; Fischer and Fischer, 1959; and Cullen and Sundsmo, 1974). At present, the question of/increased risk of cancer in anaesthetists is uncertain although a mechanism can be proposed.

an

Hepatitis

The complex controversy about the possible hepatotoxicity of halothane (Simpson, Strunin and Walton, 1975) coupled with the widespread use of the /...

agent leads inevitably to conjecture about the susceptibility of anaesthetists to develop liver disease. There is at least one anaesthetist who is presumed to have developed hepatitis as a "sensitivity" to halothane exposure (Klatskin and Kimberg, 1969). The precise mechanism for the direct hepatotoxicity of halothane is not known but halothane may be transformed in the body to metabolites which are themselves hepatotoxic (Dollery, 1972). An improved drug metabolising ability, as demonstrated by an improved rate of plasma antipyrine clearance, which has been attributed to operating theatre workers, presumed to signal risk to such persons (Wood, O'Maley and Stevenson, 1974), may in fact be evidence of adaptation on the part of the organism.

Viral hepatitis, particularly hepatitis B, is a considerable hazard in many branches of hospital practice and it is likely that anaesthetists who handle blood and saliva and are in more immediate contact with the patient than many other doctors are specially at risk (Waterson, 1976 - in press).

Conclusions

There is no doubt that operating theatres are contaminated with anaesthetic gases and that these gases are taken into the tissues of operating theatre personnel. The known influences of general anaesthetics on cell division and the demonstration of their teratogenicity in experimental animals, coupled with their known ability to cause foetal death in pregnant animals, appears to justify anxiety about the fate of pregnant women who work in operating theatres. The early survey findings, while pointing to an increase in spontaneous abortion in pregnant women who undertake anaesthetic practice are generally inconclusive. Previous reports of other health hazards in operating theatre personnel are either inconclusive or unconvincing. An increase in the incidence of liver damage either as a /...

result of exposure to halothane or, more probably, as a result of exposure to a virus seems likely.

CHAPTER 2 THE FIRST U.K. SURVEY

General Considerations and Objectives

By the autumn of 1970, the hypothesis that operating theatre work was associated with obstetric mishap was known widely. It happened that, over a two year period, there had been five live births and four spontaneous abortions among women anaesthetists in the West of Scotland. In the course of six months, three Registrars had sought advice from the author about the desirability of leaving anaesthetic practice in anticipation of becoming pregnant. Clearly, no objective opinion could be given in view of the unsatisfactory nature of the data on which the hypothesis had been based and a controlled survey of the obstetric history of women anaesthetists in the United Kingdom seemed to be essential. We commenced this work at the beginning of 1971.

The primary aim was to establish whether the frequency of spontaneous abortion was greater among anaesthetists than among other women doctors and our second aim was to compare the patterns of congenital abnormality in the two groups. It was recognised that the reporting of abortion may be subject to bias since the term is applied by women to a range of events varying from mid-cycle bleeding without significant incapacity, in women who have not had a firm diagnosis of pregnancy, to hospital admission for curettage and histological examination of the products of conception.

This problem could be reduced by asking about involuntary infertility and about the maturity of the abortion but it was decided not to seek the detailed history of the abortion. Similarly, we were aware of the possible effects of parity, maternal age, smoking habits, rubella and exposure to radiation on abortion and congenital abnormality but we decided not to seek information on these aspects also.

The reason for limiting our enquiry was that we had the opinion of several obstetricians that an enquiry of this type would be regarded as an unnecessary intrusion of privacy and that the women would be unlikely to reply. A straw-poll of thirty women anaesthetists suggested that we might expect, at most, a reply rate of 50-60%. These considerations pointed to the need for the minimum number of questions consistent with meeting the primary objectives. Although, later, we regretted the lack of additional information, it is noteworthy that no-one informed us of their unwillingness to reply on the grounds of complexity of the questionnaire whereas such objections were received in our second survey (chapters 3 and 4) in which a more detailed questionnaire was employed.

The Questionnaires

The questionnaires are shown in appendices A (anaesthetists: blue form) and B (controls: white form). The general design is similar for both groups. After entering their name and address, the controls were asked if they had been in anaesthetic practice and if they had completed the questionnaire designed for anaesthetists. Both groups stated whether or not they had been married and entered their age at the time of reply. The anaesthetists were then asked about the number of years in which they had worked in anaesthesia, whether any part of this was part-time work and, if so, the estimated number of hours per week. They were asked also whether they were working in anaesthesia at the time of reply.

Question 7 (both questionnaires) related to all pregnancies of at least 28 weeks' duration: the maturity at delivery, stillbirth, neonatal death, the sex of the child, and the occurrence of any congenital abnormality. The anaesthetists were asked whether they were employed in anaesthesia in the first and second trimesters of the pregnancy. Question 7 was limited to the reporting of the first eight deliveries and questions 8 - 10 allowed qualification of the reply to question 7 in respect of more /...

than eight children and multiple pregnancies. The anaesthetists were asked if they had been in anaesthetic practice before the first child was born. This was designed to establish whether or not the respondent had been exposed to whatever influences anaesthetists might be subject to, even although she was not actually in anaesthetic employment during any of the pregnancies.

The question on page 3 of the form related to pregnancies which terminated before the 28th week of gestation, that is the defined limit of abortion in the United Kingdom. The respondents were asked to state the maturity of the foetus and whether or not there was either a known foetal abnormality or a known cause for miscarriage.

The last section of the questionnaires dealt with involuntary infertility. We accepted the normal criterion that the infertility should have been suffered for two years or more. The respondents were asked to state the actual duration in years, whether a cause of infertility had been determined in either herself or her husband, and whether a period of involuntary infertility had ever been followed by a pregnancy. The anaesthetists were asked if they had been working in anaesthetic practice during a period of involuntary infertility or during the first trimester of any subsequent pregnancy.

Finally, space was available for any additional comments which the respondent wished to make.

The Cohorts

(a) Anaesthetists

Since there was no national register of anaesthetists in the United Kingdom, a list of women anaesthetists had to be compiled. Because /...

home addresses are preferable to hospitals as a means of contact, we attempted to use, in the first instance, the lists of the Fellows of the Faculty of Anaesthetists, Royal College of Surgeons of England, and the corresponding Body in Ireland, and the members of the Association of Anaesthetists of Great Britain and Ireland. Although these lists are maintained accurately, sampling showed that they would be unlikely to provide a sufficient number of married women to allow confident analysis of data. Requests for assistance were sent to the secretaries of all the regional anaesthetic societies. Although this provided additional names and addresses, many secretaries wrote to inform us that their membership was not representative of the women anaesthetists in their area and one secretary was unwilling to let us have the information we required. Meanwhile, the Department of Health and Social Security and the Scottish Home and Health Department had given us access to the names on their superannuation records computer file. This enables identification of specialty, grade, sex, age and the Regional Hospital Board in whose area the doctor is employed (in the case of doctors in teaching hospitals, the hospital itself can be identified).

Thus, our final list of anaesthetists included home addresses where these could be obtained from the various membership lists, but otherwise either the Regional Boards or hospital secretaries acted as intermediaries.

(b) Controls

The control group was taken from the Medical Register 1970, being every 8th woman who had registered with the General Medical Council's branches in England and Wales, Scotland, and Ireland. No attempt was made to separate from this sample the names of women who had been entered in our register of anaesthetists. According to the national tables /...

prepared by the Statistics and Research Division of the Department of Health and Social Security, approximately one in five women in hospital medicine in an anaesthetist. Although there is no method for making such an accurate prediction, the ratio of women anaesthetists to other women doctors is estimated to be one in ten by the Association of Anaesthetists. Thus, we predicted that about 10% of the names in our control group would be anaesthetists who would receive also the questionnaire designed for anaesthetists and we took account of this in preparing the explanatory letters.

Since our list of anaesthetists was unlikely to contain a significant number of women over the age of 60 years, in sampling from the Medical Register we excluded women who were registered before 1928. This assumed that the average age at first registration for women at that time was 23 years.

Handling of the Questionnaires

At the commencement of the exercise, we had 1,241 anaesthetists and 1,678 controls on our lists. Each received the appropriate questionnaire (appendices A and B), together with an explanatory letter (appendices C and D) and a reply paid envelope. The questionnaires were despatched at the end of May 1971.

Clear undertakings were given regarding the confidentiality of the enquiry and these were fulfilled scrupulously throughout the course of the study. Thus, all replies were opened by the author or his secretary and each reply was allocated a code number which was used in preference to the respondent's name for the purposes of subsequent identification. At all times, the replies were available only to the author and his three medical colleagues and, apart from the time at which the data was transferred to 80 column punch cards, under the supervision of the author /...

or one of his colleagues, the replies did not leave the author's office.

Four weeks were allowed for the replies to be returned, thereafter preparations were made to send the second questionnaire, a copy of the original letter and an additional letter (appendix E) to those who had not responded. This follow-up mailing was completed by the end of August 1971.

Replies (Table 3)

Of the 1241 anaesthetists and 1678 control mailings, an approximately equal proportion of names in each group [130 (10.5%) and 190 (11.3%)] had to be removed because they were not known to the Post Office and the envelopes had been returned, or because either the hospital or a private individual, often a landlady, informed us that the doctor had left the United Kingdom.

In computing the reply rate, the "not known" names together with known duplicates, anaesthetists in the control group, non anaesthetists in the anaesthetists group, deceased doctors and (two) males who had been included in error were deducted from the original total leaving 1034 anaesthetists and 1330 control names.

A total of 426 doctors did not reply. 11 wrote letters of refusal. 14 provided inadequate information and either did not reply to further enquiry or could not be traced. There were 849 (82.1%) usable replies from the anaesthetists and 1064 (80.0%) from the controls. Of these totals, approximately 90% were replies to the first mailing.

TABLE 3 Female survey. Details of questionnaires sent, and computation of reply rate.

		Anaesthetists	Controls
A.	Questionnaires sent	1241	1678
B.	Total entered in survey	1034	1330
C.	Total usable replies	849	1064
	Reply rate (C/B %)	82.1%	80.0%
Excluded (A-B):			
	Returned "not known"	130	197
	Not anaesthetists	1	-
	Anaesthetists	-	145
	Deceased	1	3
	Males	6	1
	Duplicates	69	1
	Total	207	348
(B-C):			
	No reply	176	250
	Refused	6	5
	Inadequate information	3	11
	Total	185	266

Analysis of Replies

563 (66%) anaesthetists and 828 (78%) controls were married (Table 4). The mean age of the married anaesthetists was 39.3 years compared with 41.8 years in the control group (Student's t test: $P < 0.001$). The anaesthetists had a total of 1,073 pregnancies, the mothers having worked in anaesthetic practice during or beyond the first trimester in 737 of these. There were 2,150 control pregnancies (Table 5). 893 anaesthetist pregnancies and 1,835 control pregnancies extended beyond 28 weeks. 50% of the anaesthetists' children and 51% of the control children were males. The stillbirth rates were 1.1% and 1% of pregnancies extending beyond 28 weeks. The neonatal death rate (within 4 weeks of delivery) was 1.2% and 1% of liveborn children.

The anaesthetists had a total of 180 spontaneous abortions and the controls had 315 abortions (Table 6). There was no known cause for more than 80% of these in both groups. No therapeutic abortions were reported. The ratio of abortions to total pregnancies was 16.8% for the anaesthetists as a single group and 14.7% for the controls. The difference is not statistically significant. However, separation of the pregnancies with respect to whether or not the mother was working in the first or second trimester, or both, shows that the ratio was 18.2% for working mothers compared with 13.7% for those not working. The difference between working anaesthetists and controls is highly significant ($P < 0.025$). Table 7 shows that there were no important differences between anaesthetists and controls in respect of the percentages of the cohorts suffering one abortion and more than one abortion.

Of the 599 children born alive to anaesthetists who had worked during the pregnancy, 39 (6.5%) were reported as having a congenital /...

TABLE 4 Numbers married in the two groups and mean ages.

	Anaesthetists	Controls
Total replies	849	1064
Married	563 (66%)	828 (78%)
Mean age married women (yr)	39.3	41.8
s.e.m.	0.47	0.35

The anaesthetists' mean age was significantly less than that of the controls. Student t test: $t = 4.3$; $P < 0.001$.

TABLE 5 Total number of pregnancies, pregnancies extending beyond 28 weeks gestation, sex of children, stillbirths and neonatal deaths. 563 anaesthetists, working and not working and 828 control doctors.

	Anaesthetists			Controls
	Working	Not Working	Total	
Total pregnancies	737	336	1073	2150
Total extending beyond 28 weeks	603	290	893	1835
Sex of children: Male			447 (50%)	945 (51%)
Female			446 (50%)	890 (49%)
Stillbirth	4 (0.7%)	6 (2.1%)	10 (1.1%)	18 (1.0%)
Neonatal death	10 (1.6%)	1 (0.3%)	11 (1.2%)	19 (1.0%)

TABLE 6 Data on spontaneous abortion for 563 anaesthetists, working and not working during the pregnancy, and 828 control doctors.

Cause of Abortion	Anaesthetists			Controls
	Working	Not Working	Total	
None known	113 (84%)	42 (91%)	155 (86%)	261 (83%)
Known	21 (16%)	4 (9%)	25 (14%)	54 (17%)
Total	134	46	180	315
Ratio Abortions/Total Pregnancies	134/737	46/336	180/1073	315/2150
Ratio as %	18.2	13.7	16.8	14.7

Anaesthetists at work vs controls: $P < 0.025$. Other differences N.S.

abnormality. The difference is statistically significant ($P < 0.02$). The frequency in anaesthetists not at work was 2.5% (7 children). In the control group, there were 89 children with abnormality (4.9%). At attempt has been made to classify these abnormalities as "major", that is life threatening or requiring major surgery, and "minor". It can be seen from Table 8 that there is no obvious difference between anaesthetists and controls in the proportion of minor to major abnormalities reported. Table 9 shows the major congenital abnormalities listed in relation to the function of the anatomical system involved. There is no significant difference between anaesthetists and controls in respect of any of the categories. Thus, the increased frequency of major congenital abnormalities reported by women anaesthetists is not attributable to the involvement of any particular system or function. The minor congenital abnormalities in both groups were all abnormalities of ectodermal development, such as accessory digits, naevi, etc., although this category includes items such as "port wine stains" which would be classed as disorders of the vasculature.

81 anaesthetists (14%) and 80 controls (10%) reported a period of involuntary infertility of 2 years' duration or more. 16 anaesthetists and 29 controls knew of a reason for the infertility as a result of clinical investigation of their problem. These included established disease of the reproductive system in either the husband or the wife, although a few disorders of general health, such as hypothyroidism, were included also. 12% of the anaesthetists and 6% of the controls had no known cause for their infertility. The difference between the groups is highly significant ($P < 0.001$). [Table 10]. 36 anaesthetists (44%) had a period of involuntary infertility which was followed by a successful pregnancy. In the great majority of these (92%), the respondent was working in anaesthetic practice during the time of the commencement of the pregnancy (Table 11).

TABLE 7 Number having one and more than one abortion. 563 anaesthetists, 828 controls. The replies from anaesthetists could not be analysed with respect to working/not working during the pregnancy. The differences between the groups are not statistically significant.

	Anaesthetists			Controls		
	No.	% Cohort	% All Abortions	No.	% Cohort	% All Abortions
One abortion	75	13	64	152	18	73
More than one abortion	43	8	36	57	7	27
Total	118	21	100	209	25	100

TABLE 8 Reporting of congenital abnormality of liveborn children. 563 anaesthetists analysed with respect to working or not working during the pregnancy and 828 controls. Major abnormality was defined arbitrarily as life threatening or requiring major surgery.

	Anaesthetists		Controls
	At Work	Not at Work	
Children born alive	599	284	1817
Congenital abnormality	39	7	89
% abnormality/live births	6.5% *	2.5% *	4.9% *
Major abnormality	23	4	59
Minor abnormality	16	3	30

* There is no significant difference between the control group and either of the anaesthetic groups. However, the difference between anaesthetists at work and not at work is statistically significant ($P < 0.02$).

TABLE 9 Numbers of reputed congenital abnormality with reference to the function or anatomical system involved in the case of 'major' abnormalities (life threatening or requiring major surgery). 'Minor' abnormalities were mainly ectodermal and are not sub-divided.

Congenital Abnormalities	All Anaesthetists	Controls
Major:		
Cardiac	5	11
Respiratory	2	1
Central nervous system	5	9
Behavioural	3	4
Gastrointestinal	4	11
Genitourinary	3	5
Bone and joint	2	12
Other	5	6
Total	29 *	59
Minor	19	30
Total	48 *	89

* Includes 2 children with two major abnormalities in different systems.

TABLE 10 Respondents reporting involuntary infertility of two years duration or more. "Known causes" were stated in most cases and included established disease or disorder of the reproductive system in either husband or wife. Established disorders of general health such as hypothyroidism were included also.

	Anaesthetists	Controls
Total	563	828
Infertile	81 (14%)	80 (10%)
Known cause	16	29
No known cause	65 (12%) *	51 (6%) *

* $X^2 = 12.8$; $P < 0.001$

TABLE 11 Pregnancy after infertility. Anaesthetists only.

	Yes	No
Pregnancy	36 (44%)	45 (56%)
In anaesthetic practice at time of onset	33 (92%)	3 (8%)

The design of the questionnaire did not enable the identification of the age of the mother at the time of the obstetric events reported nor was it possible to identify precisely the year in which these events occurred. Thus, the pooled information from all respondents was likely to be subject to the varying influence of changes in the standard of obstetric care over the years and the possible adverse effect of maternal age on obstetric history (Butler and Alberman, 1969). In an attempt to overcome this problem, the replies of women in the age range 25-35 years (inclusive) at the time of the survey were analysed separately. Table 12 shows that there were 581 usable replies from women in this age group. There were 265 married anaesthetists and 248 married controls. The proportion of women who are married in this younger age group was significantly greater among both anaesthetists and controls ($P < 0.01$) for both groups.

Within this younger age group, there were 43 abortions in women anaesthetists who worked during the pregnancy (Table 13) [abortions/total pregnancies = 19.1%] compared with 12 in women anaesthetists not at work (15.8%) and 56 in the controls (13.1%). There is no significant difference in the proportion of abortions to total pregnancies between any of these three groups (anaesthetists at work v. controls: $P \neq 0.20$). There were 12 congenital abnormalities in the children of anaesthetists at work when pregnant (6.7%) and 24 (6.5%) in children of the control subjects. There were no abnormalities reported when the mother was not working in anaesthesia during the pregnancy. However, there is no significant difference between any of the 3 groups. The analysis of the data on involuntary infertility in this younger age group showed that 25 anaesthetists had infertility for which there was no known cause (9.4%) compared with 10 in the control group (4%). The difference is statistically significant ($P = 0.01$) [Table 14].

TABLE 12 Respondents 25 - 35 years old (inclusive) at the time of survey. General data.

	Anaesthetists		Controls	
Usable replies	286		295	
Married	265		248	
	25-35 yrs	> 35 yrs	25-35 yrs	> 35 yrs
Married	265	298	248	580
Unmarried	21	265	47	189
% Unmarried	7.3%	47%	15.9%	33.6%

TABLE 13 Analysis of data from 265 anaesthetists and 248 controls aged 25 - 35 yrs inclusive. Pregnancies, etc. Abortion and congenital abnormality.

	Anaesthetists		Controls
	At Work	Not at Work	
Pregnancies	225	76	427
Children	182	64	371
Liveborn	179	64	370
Abortions	43	12	56
Abortions/pregnancies (%)	19.1	15.8	13.1
Congenital abnormalities	12	0	24
Congenital abnormalities/ liveborn (%)	6.7%	-	6.5%

TABLE 14 Analysis of data on involuntary infertility from 265 anaesthetists and 248 controls aged 25 - 35 yrs at the time of reply.

	Anaesthetists	Controls
Total	265	248
Infertile	27	17
Known cause	2	7
No known cause	25	10
No known cause/total (%)	9.4%	4.0%

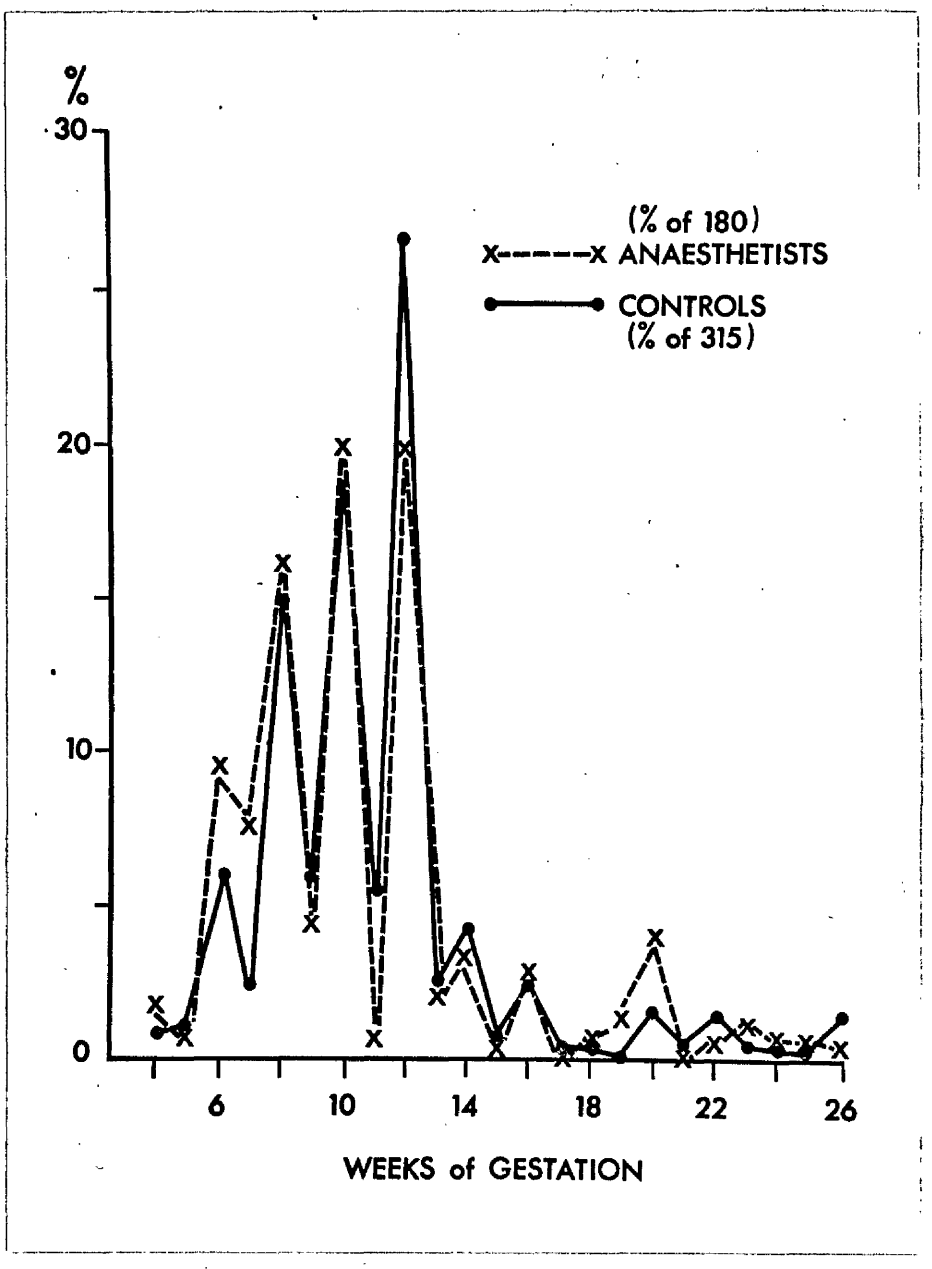


Fig.1. Abortions per cent plotted against week of gestation.

The mean maturity of the aborted foetuses in the anaesthetists (all ages) was 11.1 weeks (SEM 0.85). The corresponding figures for the controls were: mean 11.1 weeks (SEM 0.78). Figure 1 shows the distribution of percentage of abortions in each group against the weeks of gestation.

Table 15 shows the comparison of data from full-time and part-time anaesthetists and from those who had held both full-time and part-time appointments. The majority of unmarried women did not answer this part of the questionnaire and this explains the apparently high incidence of marriage in all three groups. Married women who had been working part-time exclusively had a mean age of 52.6 years, which was older than the other two groups. They appear to have a smaller frequency of spontaneous abortion, although there is no significant difference between the three groups in respect of the frequency of abortion nor is there any difference between them in respect of the proportion of liveborn children with congenital abnormalities. Women who worked in full-time anaesthetic practice exclusively had the smallest average number of children.

There was no significant difference between the anaesthetists and the controls in respect of the number of twin pregnancies and there were no reports of multiple pregnancies other than twins.

Table 15. Comparison of data from full-time and part-time anaesthetists and from those who had held both types of appointment

	Full-time	Part-time	Both
Total	271	37	286
Married	242	36	285
% married	90	97	99.6
Data from married women:			
Mean age (yr)	34.5	52.6	41.6
Pregnancies	295	108	670
Children	250	97	546
Livebirths	245	95	375
Abortions	45	11	124
Abortions/ pregnancies %	15.3	10.2	18.5
Congenital abn.	11	5	30
Cong.ab./live births%	4.5	5.3	8.0
Average children	1.0	2.7	1.9

DISCUSSION

Reply Rate

Reply rates in excess of 80% were considered to be encouraging and compare satisfactorily with the values for other large surveys of medical practitioners (Doll & Hill, 1954). It is of some interest that the addresses in the current issue of the Medical Register were of no value in 10% of cases. Confirmation of this finding was obtained in the second survey (Chapters 3 and 4) although these were undertaken after institution of the registration fee which was hoped to improve the quality of the Register as a source of reference. Some anxiety must be expressed at the fact that the proportion of married women among anaesthetists was smaller than that in the controls. This suggests that anaesthetists as a group may be different from the medical practitioners taken as a single separate group, although we can think of no obvious reasons why this should be so.

Abortion

The frequency of spontaneous abortion in anaesthetists who worked during the pregnancy was significantly greater than that of the control group. It is notable that anaesthetists who did not work during the pregnancy were closer to the controls in the reported frequency of spontaneous abortion although the difference between them and their colleagues who worked was not significant. Throughout this thesis, abortion within the United Kingdom is defined as the expulsion of the products of conception before 28 weeks of gestation. However, it is widely recognised that the diagnosis of spontaneous abortion by the patient is a highly subjective matter, notwithstanding that on this occasion the diagnosis was made by medical graduates. Thus, data is strengthened by a knowledge of such facts as the reasons for diagnosing pregnancy, the circumstances of the abortion and whether or not histological examination of the products of conception was obtained. No such information was available to us. The frequency of/...

spontaneous abortion in the community at large is difficult to determine but figures in the region of 15% have been given as an average (Roth, 1963; Warburton and Fraser, 1964). The frequency of spontaneous abortion is influenced by a number of factors including maternal smoking habits (Yerushalmy, 1971; Russell, Taylor and Law, 1968), maternal age (Havert, 1957) and perhaps also parity. Although there was a significant difference in the mean ages of the two groups, the anaesthetists were the younger group so that their high rate of spontaneous abortion is unlikely to be explained on the basis of the age factor. We had no information on the smoking habits or the parity of the mothers in relation to the abortion history.

The percentage of women anaesthetists who had a spontaneous abortion is fewer although this fact is difficult to interpret since the total number of pregnancies was less also (averages: anaesthetists 1.9, controls 2.6).

Although there is no direct evidence, Hertig and Rock (1949) have pointed to a possible association between spontaneous abortion and abnormality of the foetus. Abortions in association with chromosome abnormalities are thought to occur relatively early in the pregnancy (8th to 16th week). Thus it is tempting to suggest that an increase in the proportion of foetal abnormalities would result in the anaesthetists having a lower value for the mean maturity of the aborted foetus than that of the controls. Although such a finding was obtained in the study of Cohen, Bellville and Brown (1971) no such result emerged from the present study (figure 1).

Congenital Abnormality

Although there was a greater number of congenital abnormalities reported by anaesthetists who worked during the pregnancy compared with/...

the control group, the difference is not statistically significant. The difference between the rate for working anaesthetists and that for anaesthetists not working during the pregnancy is statistically significant although the number in the latter group is small. Although the division of congenital abnormalities into "major" and "minor" is arbitrary, it was felt that the value of the exercise lies in excluding the possibility of bias. Anaesthetists may have been more strongly motivated to describe the more trivial abnormalities such as naevi and other birth marks whereas those who were less aware of the implications of the study may have overlooked these. However, the relatively equal proportions of major to minor abnormalities in both anaesthetist and control groups suggest that there was, in fact, little bias in reporting.

The pattern of system involvement shows that the increase in the frequency of congenital abnormalities among the anaesthetists is not attributable to the involvement of any particular system: the increases occur in all categories. Thus, there is no obvious emergence of a pattern of abnormality specific to the skeletal system such as is observed in the demonstrations of anaesthetic teratogenicity in animals and such as occurred in man as a consequence of thalidomide.

Infertility

There was a clear difference in the frequency of infertility between anaesthetists and controls. Although it is difficult to obtain an accurate figure for the frequency of involuntary infertility, the typical figure of about 10% (Baird, 1962) lies between the two values which we obtained. 44% of the anaesthetists who complained of infertility had a successful pregnancy subsequently. Nearly all of these women were engaged in anaesthetic practice at the time of the onset of the pregnancy, thus suggesting that operating room exposure is not an exclusive factor.

Design of the Questionnaire

Although it was felt that the policy, of reducing to a minimum the number of questions included in the questionnaire, was justified, there can be no doubt that the enquiry was deficient in that it was not possible to relate the obstetric events to the year in which they occurred or to the age of the mother at the time of the pregnancy. Earlier reference has been made to the lack of information regarding the abortions and the smoking habits of the mother. Information was lacking also on other factors which might contribute to foetal abnormality and either subsequent spontaneous abortion or congenital abnormality of liveborn children. These include previous contraceptive history, previous rubella and exposure to x-rays.

The information supplied on congenital abnormality was of a very general nature. There were no detailed or objective evaluations such as might have been possible had the children been examined by paediatricians. Moreover, there was no method of eliminating bias in reporting although there is no reason to suspect that this was a serious problem.

On the positive side, the small number of questions is thought to have contributed to the high reply rate and it is noteworthy that only very few of the women who were questioned had any difficulty in understanding or completing the questionnaire.

Analysis of Replies from Women Aged 25-35 Years

This analysis was an attempt to overcome lack of information about maternal age and the year of birth, the assumption being that replies from women in this age range would exclude adverse factors operating in older women together with such influences as might have resulted from changes /...

in the patterns of obstetric care over the years.

Although there were no significant differences between the groups, women who worked during the pregnancy had more abortions than those in the other groups, and indeed the difference between working anaesthetists and controls is greater in this analysis than when all the data were pooled.

By contrast, the frequency of congenital abnormalities (exposed anaesthetists versus unexposed) were almost identical. However, in this analysis as in the analysis of the pooled data, involuntary infertility was about twice as frequent in the anaesthetists as in the control group.

Conclusions

On balance, the data resulting from this study are in agreement with the trends in the previous studies of the frequency of spontaneous abortion associated with anaesthetic practice, although the estimate of the size of the risk is much less. Cohen, Bellville and Brown (1971) estimated that the risk was increased three-fold. On the basis of our pooled data, we would estimate the increase to be 24% or, at most, (on the basis of the analysis of the younger age group alone) about 46%.

Taken together, the triad of an increase in the rate of spontaneous abortion, congenital abnormality and involuntary infertility in working anaesthetists suggests the common factor of foetal abnormality presenting either as a very early abortion, manifested as involuntary infertility, or a frank spontaneous abortion, or as a full-term pregnancy with consequent congenital abnormality. Against such a hypothesis, which otherwise would seem to be strong evidence of a toxic effect of anaesthetic pollution, is the fact that the mean maturity of the abortions was not influenced, that the pattern of congenital abnormalities was not consistent with a teratogenic/..

influence, and that the involuntary infertility was not necessarily refractory even when the women continued to work in anaesthetic practice.

If it is accepted that the data on spontaneous abortion and involuntary infertility is valid, other factors such as the patterns of work, the possible influence of "stress", effects of lifting patients and bending, and the general features of the life style of the working anaesthetist such as the possible increase in smoking habits and coffee drinking cannot be excluded.

Suggested Further Action

As a result of these findings, the following further action seemed either possible or desirable:

1. A more detailed survey of the same women as had been included in the original survey. It was felt that this was not advisable since such a course would be likely to cause irritation which might seriously affect the reply rate.

2. A similar survey of the wives of male anaesthetists having regard to the findings of Askrog and Harvald (1970). A positive finding in that group also would lend strong support to the pollution hypothesis.

3. A prospective survey of women anaesthetists. Such a course would be more acceptable from the epidemiological stand-point since retrospective surveys are generally regarded as the least reliable method of obtaining data of this type. However, there was uncertainty as to the necessary duration of a prospective survey. Some estimates suggested that a 10 year period would be required and,in view of the urgency of the problem, it was felt that all possible other means should be explored.

4. A detailed prospective survey of the histological findings of abortuses. Although such an idea would be considered appropriate by many (Carr, 1971)/...

practical difficulties in the way of such a course seemed impossible.

General Attitudes to These Data

A summary of the main findings of this enquiry was published (Knill-Jones, Moir, Rodrigues and Spence, 1972) and this report evoked a certain amount of reaction in both the medical and lay press [Editorial, 1972(a), (b) and (c)]. In most cases, the implications of the findings were taken seriously and it was felt that the possibility of a risk resulting from operating room pollution could not be excluded. This led to uncertainty of attitudes in women who worked in anaesthesia. Most married women appeared to be ready to accept such risks as existed although a few, who had experienced obstetric difficulty in the past, elected to leave anaesthetic practice and in most cases their reasons for doing so were accepted with understanding. At the same time, there was no clear guide from the data in the study to indicate whether such a course of action would be beneficial.

Finally, the attitude in response to the results of this survey were an important stimulus to the development of techniques for reducing the levels of pollution in operating theatres (Vaughn et al, 1973).

CHAPTER 3 THE SECOND UNITED KINGDOM SURVEY

MALE DOCTORS

Purpose

In view of the finding that women who practice anaesthesia appeared to be susceptible to spontaneous abortion and involuntary infertility, and that they might also be more likely to produce children with congenital abnormalities, it was important to determine whether a similar pattern applied also to the wives of male anaesthetists even although these women had not worked in an operating theatre. It was considered that a positive finding might suggest an abnormality of spermatogenesis and this would support the pollution hypothesis. On the other hand, a negative finding might help to allay growing anxiety, among those who were working in operating theatres, that atmospheric pollution with anaesthetic gases is harmful.

This is a report of a survey of male anaesthetists and non-anaesthetist male doctors in the United Kingdom with particular reference to the obstetric history of the marriages.

Method

Questionnaires were sent to all Fellows in the Faculty of Anaesthetists, members of the Association of Anaesthetists, and anaesthetists on the 1972 superannuation records of the Department of Health and Social Security and the Scottish Home and Health Department. Whenever possible, an attempt was made to find the doctor's home address with the aid of the Medical Register, 1972. A list of doctors was prepared by taking every 10th male doctor, resident in the United Kingdom, from the Register. Thereafter, the various lists were checked to ensure that a doctor's name did not appear more than once. In sampling names from the Register, doctors who qualified before 1932 were excluded in an attempt to ensure that all/...

respondents were not more than 65 years of age at the time of the survey.

One questionnaire and a reply paid envelope were sent to each doctor on the lists. No name was attached to the forms, although a code number served to identify the respondents so that a follow-up questionnaire could be sent to those who had not replied within 3 months. The first batch of replies and the replies from the follow-up questionnaires were analysed separately in the first instance. As in the previous enquiry, complete confidentiality was ensured.

This enquiry was conducted in collaboration with the American Society of Anesthesiologists' Ad-Hoc Committee on the Effect of Trace Anaesthetics on the health of operating room personnel. The Committee's preliminary findings were published in October 1974 (Cohen et al, 1974). Because of differences in the understanding of terminology, there were minor differences between the British and American questionnaires but the nature of the questions and the general design of the reply forms was similar for the two countries.

The Questionnaire (Appendix F)

The questionnaire was in 4 sections. Section 1 enquired about infertility which was defined as a period of involuntary infertility of two years or more. The section was designed to elicit whether there was a known cause of infertility, whether a period of infertility had been followed by a pregnancy, and whether infertility or a subsequent pregnancy had coincided with a period of employment in an operating theatre.

The second section related to the history of each pregnancy, including the age of the mother at the time of the pregnancy, whether or not she smoked cigarettes, suffered rubella, or had been subjected to abdominal/...

x-ray during the pregnancy. Questions were asked about exposure of either parent in an operating theatre in any of the trimesters of the pregnancy, the weight and maturity of a liveborn baby, whether or not there had been stillbirth or abortion and the estimated maturity of the foetus in the event of either of these. Respondents were asked about the nature of any congenital abnormality of liveborn children and about the subsequent health of all children. They were asked also to state whether any child had died and, if so, the cause of death.

A third section asked about the occupation of the respondents in each of the last 10 years, the following categories being recognised: anaesthetists, surgeons, radiologists, other hospital employment and non-hospital employment. The last section of the questionnaire related to diseases of respondents themselves. Data from this part of the enquiry are presented in Chapter 4.

Analysis of Data

All the data were coded and transferred to 80 column punch cards. The data on obstetric history were analysed according to whether or not the respondent was working in an operating room ("exposed") in the first trimester of the pregnancy. Thus, no attempt was made to separate replies from anaesthetists and surgeons within the exposed group. Although the survey was designed to assess a possible effect of male exposure in an operating room, the data included a number of pregnancies where either the mother and father, or the mother alone, had been exposed. Thus, we had an opportunity to re-examine the possible influence of maternal exposure in the light of our earlier enquiry (Knill-Jones et al, 1972).

Response

The questionnaire was sent to a total of 7949 doctors of whom 5569 replied, giving 5507 usable replies (Table 16). 5119 (93%) of the respondents were married and 4602 (84%) reported one pregnancy or more. The distribution with respect to principle type of employment was: anaesthetists 26%, surgeons 9%, radiologists 1%, other hospital staff 17%, non hospital doctors 39%, miscellaneous or retired 8%.

A comparison of replies to the first and second mailings with respect to the principle data is given in Table 17, which shows no important differences in the pattern of replies between the two mailings. The first mailing yielded details of 11579 pregnancies and the second 2131 pregnancies.

RESULTS

Abortion

Table 18 shows the data relating to spontaneous abortion. In this and subsequent tables, the term "exposed" is used to signify that the respondent or his wife was working in an operating theatre in either the first, or the first and second trimester of the pregnancy. There was no apparent influence of paternal exposure on the frequency of spontaneous abortion (exposed 11.1%, not exposed 10.9%). However, exposure of the mother was associated with a frequency of abortion of 15.5% compared with 10.9% where neither parent was exposed. Although the total number of pregnancies in which the mother was exposed is small in relation to the other data in Table 18, the apparent effect of maternal exposure is highly significant ($X^2 = 9.9$; $P < 0.01$). There was no obvious effect of exposure on the mean maturity of the abortions: no exposure 11.2 weeks, father exposed 10.9 weeks, mother exposed 11.2 weeks. Table 19 shows /...

TABLE 16 Survey of male doctors : mailing data and reply rates

	1st mailing	2nd mailing	Total
Total sent *	7949	3597	7949
Returned not delivered	823	277	1100
Useable replies	4639	868	5507
Unuseable replies **	44	18	62
Total replies % ***	56.9	26.7	70.1

* Excludes duplicates and doctors found to be either female or deceased

** Refusals, incomplete and late replies

*** Questionnaires not delivered have been subtracted from the total sent

TABLE 17 Survey of male doctors : comparison of replies to 1st and 2nd mailings. There are no significant differences between 1st and 2nd mailings except for reporting of miscellaneous diseases.

	1st Mailing	2nd Mailing
Married (% total replies	93.3	91.0
1 pregnancy or more (% married)	90.1	88.7
'Exposed' during 1st trimester (% pregnancies) (mother or father)	47.3	44.2
Abortions " "	11.2	10.9
Stillbirths " "	0.92	0.76
Congenital Abnormality (% live births):		
Total	4.0	4.4
Major	1.0	1.5
Minor	3.0	2.9
Maternal Factors (% pregnancies):		
Smoking	30.0	33.3
Rubella	0.51	0.84
X-ray	11.5	12.8
Children:		
Deaths (% live births)	182 (1.8)	38 (2.0)
Cancer	26 (0.26)	9 (0.48)
Infertility:		
Total (% married replies)	484 (11.2)	94 (11.9)
Known cause	186 (4.3)	34 (4.3)
Theatre exposure	219 (5.1)	47 (5.9)
Disease in Respondents:		
Cancer	73 (1.6)	19 (2.1)
'Kidney'	106 (2.3)	25 (2.9)
'Liver'	105 (2.3)	24 (2.8)
(Other'	587 (12.6)	136 (15.7)

TABLE 18 Male survey. Details of spontaneous abortion showing no apparent effect of paternal exposure and a significant increase associated with maternal exposure ($X^2 = 9.9$; $P < 0.01$)

	Pregnancies	Spontaneous Abortions	$\frac{\text{Abortions}}{\text{Pregnancies}}$ (%)
Exposure:			
Father	5891	657	11.1
Neither	7296	795	10.9
Father and Mother	357	51	14.3
Mother	166	30	18.0
Maternal exposure (total)	523	81	15.5

TABLE 19 Male survey. Frequency of abortion related to total number of prenancies. Analysis of 1st and 2nd pregnancies with respect to paternal or maternal exposure in an operating theatre.

	Total Pregnancies	Spontaneous Abortions	$\frac{\text{Abortions}}{\text{Total Pregnancies}}$ (%)
FIRST PREGNANCY			
Exposure:			
Male	1856	142	7.6
Female	353	57	16.1
Neither	2393	184	7.7
SECOND PREGNANCY			
Exposure:			
Male	1799	173	9.6
Female	98	11	11.2
Neither	2162	200	9.2
THIRD & SUBSEQUENT PREGNANCIES			
Exposure:			
Male	2593	393	15.2
Female	72	13	18.1
Neither	2907	441	15.2

Female exposure v. neither : 1st pregnancy $X^2 = 26.4$; $P < 0.001$

2nd pregnancy $X^2 = 0.23$; N.S.

the analysis of the first and second pregnancy. In both analyses, male exposure was not associated with an increase in the frequency of abortion. Female exposure in the first pregnancy was associated with a 16.1% frequency of abortion compared with 7.7% where there was no exposure ($X^2 = 26,4$; $P < 0.001$). The corresponding values for the second pregnancy were 11.2% and 9.2%, a difference which is not statistically significant ($X^2 = 0.23$).

Congenital Abnormality

Table 20 shows the frequency of reported congenital abnormalities of liveborn children. Where possible, we have attempted to describe these as "major", that is life threatening, resulting in either major surgery or serious disability, and "minor". Both male exposure and non-exposure were associated with approximately a 1% frequency of major abnormalities. Female exposure was associated with a frequency of 1.59%, although this represents only 7 children and the apparent difference associated with female exposure is not statistically significant. There was a statistically significant increase in the reporting of minor abnormality associated with male exposure (3.09%) compared with pregnancies in which there was no exposure (2.35%) ($X^2 = 5.61$; $P < 0.02$). Female exposure was associated with a frequency of 3.19%: this represents only 14 children and the value is not significantly different from that associated with no exposure. The frequency of reporting of all abnormalities (including some which could not be classified as major or minor) in exposed females is 5.5%, compared with 3.6% in non-exposed pregnancies. This is not statistically significant. ($X^2 = 3.5$; $P > 0.05$). However, the abnormality rate of 4.5% associated with male exposure is significantly higher than in the non-exposed group ($X^2 = 6.1$; $P < 0.05$).

Table 21 lists all abnormalities in relation to type or the anatomical/...

TABLE 20 Male survey. Number of liveborn children and those with congenital abnormality. Data presented with respect to paternal and maternal exposure in an operating theatre.

	No. of Children	Major Abnormality (%)	Minor Abnormality (%)	Total Abnormalities *
Exposure:				
Male	5175	56 (1.08)	160 (3.09)	235 4.5%
Female	438	7 (1.59)	14 (3.19)	24 5.5%
Neither	6442	58 (1.05)	152 (2.35)	233 3.6%

* Note: Inoludes 35 abnormalities which could not be assigned with confidence to the "major" or "minor" categories.

Minor abnormality: male exposure v neither: $X^2 = 5.61$; $P < 0.002$
female exposure v neither: N.S.

Total abnormality: male exposure v neither: $X^2 = 6.1$; $P < 0.05$
female exposure v neither: N.S.

TABLE 21 Types of congenital abnormality reported. Number of children and percentage of total abnormalities in two groups: non exposed and exposed father or mother

	Non exposed	Exposed	X^2
Cleft Palate	7 (3.0%)	7 (2.7%)	-
Skeletal	61 (26.2%)	69 (26.6%)	-
C.N.S.	35 (15.0%)	40 (15.4%)	-
Gut	14 (6.0%)	19 (7.3%)	-
Cardiovascular/respiratory	33 (14.2%)	24 (9.3%)	2.4 N.S.
Genitourinary	28 (12.0%)	20 (7.7%)	2.1 N.S.
Endocrine	2 (0.8%)	4 (1.5%)	-
Mental retardation	13 (5.6%)	19 (7.3%)	-
Skin	27 (11.6%)	35 (13.5%)	-
Unspecified/multiple	13 (5.6%)	22 (8.5%)	1.2 N.S.
Total	233	259	

system involved. There were no significant differences between pregnancies in which there had been no exposure and those in which one or both parents had been exposed.

Stillbirth and Death

When either parent had been exposed during the pregnancy, there were 63 stillbirths out of a total of 6414 (0.98%) compared with 59 out of a total of 7296 (0.80%) for non-exposed parents. The difference is not statistically significant.

There was no apparent influence of parental exposure in an operating theatre on the frequency of death of children at any time after birth (1.85% for both exposed and non-exposed groups), or in the frequency of cancer or leukaemia in children (exposed 0.20%; non-exposed 0.26%).

Infertility

117 (9.7%) anaesthetists, 132 (10.6%) other hospital doctors and 234 (10.8%) doctors not working in hospital reported involuntary infertility of not less than two years' duration. There is no significant difference between these three groups of male doctors.

Matched Data

In calculating the data presented in Tables 18 to 20, no allowance was made for some of the information which was available in the replies and which is likely to affect the frequency of spontaneous abortion, congenital abnormality and stillbirth. Therefore, we have matched pregnancies with respect to maternal smoking habits, birth order and maternal age at the time of birth. 4074 (69.2%) of all pregnancies in which male exposure/...

had occurred were matched successfully with pregnancies in which there was no male exposure. There were 1090 pairs of smokers (26.8%), the mean maternal age, matched to within 2 years, was 28.9 years and the mean year of the father's birth, matched to within 2 years also, was 1927. Of the 4074 pairs, 34.2% were first pregnancies and 32.1% were second pregnancies. The frequency of spontaneous abortion, congenital abnormality and stillbirth is shown in Table 22. There was no statistically significant difference in the frequency of spontaneous abortion between the exposed group (10.6%) and the non-exposed group (9.8%). A 4.5% frequency of all types of congenital abnormality in the exposed group was significantly greater than that reported by the non-exposed group (3.2%) ($X^2 = 7.6$; $P < 0.01$) and this is explained largely by an increase in the reporting of minor congenital abnormality by the exposed group. There was no obvious effect of exposure on the stillbirth rate.

Table 23 shows corresponding data with a similar matching of pregnancies except for exposure of the female. 435 (83.2%) of all the female exposed pregnancies were matched successfully with respect to maternal smoking, birth order, maternal age at the time of birth and paternal age at the time of response (both ages to within 2 years). There were 151 (34.7%) pairs of smokers, the mean maternal age was 27.6 years and the mean paternal year of birth was 1931. Of the 435 pairs, 68.1% were first pregnancies and 19.3% were second pregnancies. There is a striking difference in the frequency of spontaneous abortion in the exposed group (14.9%) compared with the non-exposed group (5.5%) ($X^2 = 20.0$; $P < 0.001$). The exposed group were found to have a significantly greater frequency of all types of congenital abnormality, which is attributable to an increase in the reporting of both major and minor abnormalities. However, it should be noted that in this analysis the total number of children with congenital abnormality is small. In order to increase the numbers in the control group, and as an additional check, each exposed pregnancy was matched with two /...

TABLE 22 Survey of male anaesthetists. Results of retrospective matching of data : male exposure. 4074 pairs of pregnancies matched except for male exposure/ no exposure. Abortions and stillbirths given as percentage of total pregnancies.

	Exposed	Not Exposed	X^2	P
Abortions	10.6% (433)	9.8% (399)	1.4	N.S.
Total congenital abnormality/ total live births *	4.5% (161)	3.2% (117)	7.6	< 0.01
Major abnormality	1.06% (38)	0.93% (34)	0.2	N.S.
Minor abnormality	3.1% (111)	2.1% (78)	6.0	< 0.02
Stillbirths	0.86 (35)	0.64 (26)	1.1	N.S.

* Total live births, exposed 3597, not exposed 3642.

TABLE 23 Male survey. Results of retrospective matching of data: female exposure. 435 exposed pregnancies matched (1:1) with controls

	Exposed	Not Exposed	X^2	P
Abortions	14.9% (65)	5.5% (24)	20.0	< 0.001
Total congenital abnormality/ total live births	5.5% (20)	1.5% (6)	8.4	< 0.01
Minor abnormality	3.3% (12)	1.0% (4)	4.2	< 0.05
Stillbirths	0.92% (4)	0.46% (2)		

Total live births, exposed 366, not exposed 408.

controls. Thus, Table 24 shows corresponding data for matching of one exposed female to two controls. 73.8% of the pregnancies were matched successfully. This type of matching exercise (1:2) was repeated after altering the order of cases in the files: the results are in Table 25. The proportion of smokers, the mean ages and the distribution of birth orders was similar to that in Table 23.

These analyses show also a clear increase in the frequency of spontaneous abortion associated with exposure in an operating theatre. However, no significant difference between exposed and non-exposed pregnancies was revealed in the frequency of congenital abnormalities.

DISCUSSION

The reply rate of just more than 70% was less satisfactory than that of the earlier survey of women doctors (Chapter 2) in which the rate was more than 80%. Initial separate analysis of replies to the first and second mailings in the present survey showed that there were no important differences between these and it is assumed from this that the replies which were received are representative of all the doctors who received questionnaires. Several doctors wrote to say that the questionnaire was too complex for them and it may be that the relatively large number of questions had an effect in reducing the reply rate.

Abortion

The results of this survey suggest that male doctors who work in operating theatres do not incur any additional risks in respect of the obstetric history of their marriage. Thus, the earlier report by Askrog and Harvald (1970) that the wives of male anaesthetists may suffer an increased frequency of spontaneous abortion is not confirmed. The recent/...

TABLE 24 Male survey. Results of retrospective matching of data: female exposure. 386 exposed pregnancies matched (1:2) with controls

	Exposed	Not Exposed	X^2	P
Abortions	14.5% (56)	9.2% (71)	6.9	< 0.01
Total congenital abnormality/ total live births 2/	5.3% (16)	4.9% (37)	0.02	N.S.
Minor abnormality	3.4% (11)	3.3% (23)		
Stillbirths	1.0% (4)	0.8% (6)		

Total live births, exposed 326, not exposed 693.

TABLE 25 Male survey. Results of retrospective matching of data: female exposure

As for Table 9 but with an alternative order of files giving a substantially different control group. Abortions and stillbirths are given as % total pregnancies.

	Exposed	Not Exposed	X^2	P
Abortions	14.8% (57)	7.0% (54)	17.0	< 0.001
Total congenital abnormality/ total live births 3/	4.9% (16)	4.9% (35)		
Minor abnormality	3.4% (11)	3.2% (23)		
Stillbirths	1.0% (4)	0.8% (6)		

Total live births, exposed 325, not exposed 710.

American Ad Hoc Committee study also found no influence on the frequency of abortion which might be attributed to male exposure (Cohen et al, 1974). Thus, it is tempting to suggest that Askrog's findings were the result of other factors, the most obvious being the effect of age on spontaneous abortion since they compared obstetric history before and after commencing employment in anaesthesia; there was no control group.

Congenital Abnormality

The results of both the matched and unmatched data show that there is an increased frequency of congenital abnormality of liveborn children associated with male exposure. This is attributable to an increase in the frequency of minor abnormalities. The distribution of abnormalities is in broad agreement with the data of Davie, Butler and Goldstein (1972) for the general population.

In our opinion, the apparent small effect of male exposure on congenital abnormality should be interpreted with caution. At the time of replying to this questionnaire, many anaesthetists, surgeons and others who work in operating theatres were already aware of possible health hazards associated with operating theatre employment and the reporting of minor congenital abnormalities may be more susceptible to bias than is the reporting of more major problems. It should be noted also that the increased reporting by exposed male doctors relates to all anatomical systems equally. Thus, there was no specific system involvement such as might be expected in the event of a toxic drug effect (Chapter 1). The conclusion that male exposure does not influence congenital abnormality may be different from that of the Ad Hoc Committee in the United States. They found a trend towards an increase in the reporting of abnormalities where the father had been exposed and in one of their several groups, this reached the level of statistical significance. They did not distinguish major and minor abnormalities but they excluded skin anomalies completely. There was a clear increase in the occurrence of multifactorial abnormalities among the wives of male respondents/.

(1.56%) compared with controls (0.90%) ($P < 0.03$) in the American study but not in the U.K. study.

Matched Data

It is of considerable interest that anlysis of the present data with respect to exposure of the mother in an operating theatre in the early part of the pregnancy confirmed the earlier findings that female exposure is associated with an increased frequency of spontaneous abortion. Unfortunately, it is not known what proportion of the replies in this second survey relate to the same women who replied in the first survey (Chapter 2), nor is it known the proportion of doctors to nurses among the wives of the respondents in the present survey. Nevertheless, the findings are consistent and are in broad agreement with both an earlier (Cohen, Bellville and Brown, 1971) and the more recent enquiry in the United States (Cohen et al, 1974).

The matching of the data appears to highlight the risk associated with maternal exposure. In Tables 23, 24 and 25, the non-exposed abortion frequency ranges from 5.5% to 9.2% (values less than the average for the study because of the high proportion of first pregnancies in which the abortion rate is known to be low compared with subsequent pregnancies) whereas the exposed abortion rates range from 14.5% to 14.9% representing an estimated increase in the risk ranging from 158% to 271%.

The results of the first U.K. Survey (Chapter 2) suggested a possible increase in the frequency of congenital abnormality associated with maternal exposure. However, analysis of the present data does not support this except for a possible increase in the reporting of minor congenital abnormalities to which we believe our cautionary remarks made above apply. The U.S. Ad Hoc Committee's report (Cohen et al, 1974) shows an apparent effect/...

of maternal exposure on congenital abnormality. There is no clear explanation for this difference between our present study and the U.S. study. However, a more detailed comparison of the British and American dats is given in Chapter 5.

In this analysis, it was considered more appropriate to investigate the effects of exposure, rather than the practice of anaesthesia which was the criterion for the test group in the first U.K. study. Although the difference between these categories is not substantial, these enquiries are related to the possible harmful effects of operating theatre contamination with anaesthetics. It was considered reasonable to expect that some of the anaesthetists would, in fact, work outside the operating room while some of the non-anaesthetists would have been exposed. Unfortunately, we were unable to make this distinction in the first U.K. study.

Table 26 combines data from the first and second U.K. studies which suggest a reasonable level of agreement between the two. Table 27 compares data on involuntary infertility from the two studies. The reported frequencies are remarkably similar in all the groups with the exception of the women anaesthetists in whom there is an obvious increase.

TABLE 26 Female exposure in an operating room. Effect on various aspects of child-bearing. Comparison of data from U.K. female anaesthetists study (Chapter 2) and data of exposed females obtained in the course of the U.K. male study. 'Female anaesthetist' and 'exposed female' are not necessarily synonymous.

	Female Study 1971	Male Study 1973
Abortion (%):		
Exposed women or anaesthetists	18.2	15.4
Controls	14.7	10.9
Congenital Abnormality:		
Exposed women or anaesthetists	6.5	5.5
Controls	4.9	3.6
Stillbirth:		
Exposed women or anaesthetists	0.70	0.64
Controls	1.00	0.80

TABLE 27 Infertility. Comparison of data from the two U.K. surveys. Exposure signifies female (1971) or male (1973) working in operating room in association with a period of involuntary infertility.

Infertility	Female Study 1971	Male Study 1973
Total:		
Exposed	81 (14%)	137 (9.7%)
Controls	80 (10%)	158 (10.7%) 281 (10.8%)
No Known Cause:		
Exposed	65 (12%)	83 (5.9%)
Controls	51 (6%)	92 (6.2%) 183 (7.1%)

CHAPTER 4 SECOND U.K. SURVEY.

ILLNESS IN MALE RESPONDENTS

Introduction

It has been noted already that the form of questionnaire employed in the second U.K. survey was designed in collaboration with the American Ad Hoc Committee. Because of previous American findings, discussed in Chapter 1, which suggested that there may be an abnormal pattern of morbidity among anaesthetists in the United States, our American colleagues were anxious to include a short section regarding the general health of the respondents and it was agreed that a similar section would be incorporated in the British study of male anaesthetists.

It should be emphasised that this part of the enquiry was regarded as a pilot study only. Thus, the form was designed to elicit information about three categories of disease: cancer, liver disease, and kidney disease, although the opportunity was given for the respondents to report any other major health problems which they had experienced. The intention was to seek information relating to the previous 10 years only.

Although section 3 of the enquiry form allowed reports of illness to be related to 5 different work categories, in practice the numbers in some of the categories were so small that in the presentation of data which follows 3 categories only have been used; anaesthetists, other hospital doctors, non hospital doctors.

RESULTS

Table 28 shows the percentage of doctors reporting ill from the different medical practice categories and for 4 decades of age. Allocation to the practice categories made on the basis of the doctor having been employed/...

TABLE 28 Male survey. Age and % Reporting Ill by Occupation. All Respondents. Total Number of Respondents Bracketed.

Medical Practice	Age years 57 - 66	47 - 56	37 - 46	< 37
Anaesthetists	39.5% (210)	31.0% (371)	15.6% (520)	14.7% (306)
Surgeons	35.3% (85)	25.5% (98)	11.4% (158)	11.9% (151)
Radiologists	23.8% (21)	5.0% (20)	8.3% (24)	10.0% (10)
Other Hospital Staff	26.6% (113)	15.7% (204)	15.9% (220)	9.9% (374)
Outside Hospital	27.0% (415)	20.4% (747)	12.9% (651)	13.1% (313)
Mixed Category/Retired	30.0% (20)	41.7% (12)	21.1% (19)	6.5% (414)

in one of the categories for the previous 4 years or more. Thus, a relatively large number of those in the under 37 age group could not be placed.

There was a tendency for anaesthetists to report illness more frequently than did the other groups, although none of the differences between the anaesthetists and the next highest category in any of the columns of Table 28 was statistically significant. Table 29 shows the numbers reporting 1, 2, 3 or 4 diseases simultaneously. Single disease reporting was commoner among anaesthetists (18.2%) compared with other hospital doctors (12.2%) [$X^2 = 19.9$; $P < 0.001$]. The reporting of more than one disease at a time in anaesthetists (2.3%) was not significantly greater than in other hospital doctors (1.6%) or in non-hospital doctors (1.85%).

Table 30 shows the reported disease rates for all respondents divided into 3 work categories. The group with the highest reporting in each disease category has been underlined. There was no significant difference between the groups in respect of the reporting of cancer, kidney disease, diseases of the central nervous system and the respiratory system. Anaesthetists had a significantly greater frequency of liver disease, bone and joint disease, diseases of the cardiovascular system and diseases of the gastro-intestinal tract.

Liver Disease

Table 31 shows that more than 87% of liver diseases were diagnosed as hepatitis although the specific type of hepatitis was not given consistently.

Table 32 shows the distribution of hepatitis in the respondents, divided according to age and occupation category. Although the numbers are too small to permit statistical significance to emerge, there is a distinct pattern of reporting. The mean rates for respondents aged over and under /..

TABLE 29 Multiple disease reporting and specialty. Single disease reporting is commoner among anaesthetists (18.2%) compared with other hospital doctors (12.2%), $X^2 = 19.9$; $P < 0.001$. However, reporting of more than one disease at a time in anaesthetists (2.3%) is not significantly greater than in hospital doctors (1.6%), $X^2 = 1.3$; or non-hospital doctors (1.85%).

	Number of Diseases Reported							
	1		2		3		4	
Anaesthetists (1407)	256	18.2%	29	2.1%	3		0	
Hospital (1478)	180	12.2%	21	1.4%	3		0	
Non-Hospital (2591)	336	13.0%	37	1.4%	10	.4%	1	

TABLE 30 Male survey. Reported Disease Rates. All Replies. 5476 Respondents - Anaesthetists 1407 (25.7%), Other Hospital 1478 (27.0%), Non-Hospital 2591 (47.3%)

Disease	Anaesthetists		Other Hospital		Non-Hospital		P	X^2
Cancer	22	1.56%	25	1.69%	44	1.7%	N.S.	.1
Liver	44	3.13%	36	2.44%	49	1.9%	<.05	6.1
Kidney	31	2.2%	38	2.57%	62	2.39%	N.S.	.4
Bone & Joint	42	2.99%	16	1.08%	40	1.54%	<.001	16.5
Cardiovascular	71	5.05%	37	2.5%	106	4.09%	<.01	12.9
Gastrointestinal	68	4.8%	41	2.77%	93	3.59%	<0.02	8.74
C.N.S.	24	1.71%	15	1.01%	28	1.08%	N.S.	3.7
Respiratory	33	2.35%	20	1.35%	41	1.58%	N.S.	4.7
Miscellaneous	38	2.7%	38	2.6%	48	1.85%	N.S.	3.8

Doctor group with highest reporting rate underlined.

TABLE 31 Liver diseases reported by all respondents

	Cases	% of all liver cases
Hepatitis	113	87.6%
Glandular Fever	5	3.9%
Non-Specific	8	6.2%
Cirrhosis	2	1.6%
Gilbert	1	0.8%
	$^{129}/_{5476}$ (2.36%)	

Non-Hepatitis Cases (16)

Anaesthetists	$^{6}/_{1407}$	0.43%	
Other Hospital	$^{4}/_{1478}$	0.27%	
Non-Hospital	$^{6}/_{2591}$	0.23%	$X^2 = 1.31$, N.S.

TABLE 32 Hepatitis (type not specified) in 5476 respondents grouped according to age and occupational category. Number affected and % in each age group.

Age (yr)	Anaesthetists		Other Hospital Doctors		Non-Hospital Doctors		Total		X^2	P
	No.	(%)	No.	(%)	No.	(%)	No.	(%)		
< 37	11	3.6	10	1.9	17	2.3	38	2.4	1.96	N.S.
37-46	12	2.3	13	3.2	15	2.4	40	2.5	0.5	N.S.
47-56	11	3.0	6	1.9	8	1.0	25	1.7	5.4	N.S.
57-66	4	1.9	3	1.4	3	0.7	10	1.2	1.96	N.S.
Total	38	2.7	32	2.2	43	1.7	113	2.1	0.7	N.S.

47 years are shown in figure 2 which shows that hepatitis appears to be a problem in younger men rather than in older men (remembering that data had been collected for the previous 10 years only), and is more common in anaesthetists than in other hospital doctors who in turn have a higher frequency than doctors who do not work in hospitals.

Kidney Disease

There was no significant difference between any of the groups in respect of the reporting of kidney disease. The frequencies in each of the 3 groups were very close.

Diseases of Bones and Joints

Table 33 shows the distribution of various diseases among all the respondents. The most serious problem is that of prolapsed disc with gout in second place. The distribution of gout between the 3 occupational categories is shown in the lower part of Table 33. There is no significant difference between any of the 3 categories.

Table 34 deals with lumbar or cervical disc and associated problems. The respondents are sub-divided in relation to both age and occupation. There is a notable increase in the reporting of these problems by anaesthetists compared with the other 2 groups and the difference is especially marked in doctors under the age of 37 years.

Cardiovascular Disease

Table 35 shows the principle types of cardiovascular diseases reported and the numbers in each category. The largest numbers complained of /...

TABLE 33 JOINT DISEASE

		% of Joint Disease
Prolapsed discs	38	38.8
Gout	17	17.3
Other back problems	12	12.2
Rheumatoid arthritis	11	11.2
O.A. major joints	8	8.2
O.A. minor joints	5	5.1
Other joint trouble	6	6.1
Polymyalgia	3	3.1

$^{98}/_{5476}$ (1.79%)

	Anaesthetists	Other Hospital	Non-Hospital
Gout	$^{8}/_{1407}$ .57%	$^{4}/_{1478}$ .27%	$^{5}/_{2591}$ .19%

$X^2 = 4.24$ N.S.

TABLE 34 All lumbar or cervical disc and associated problems. All doctors (5476)

Age	Anaesthetists	Other Hospital	Non-Hospital	Total
57 - 66	$^{2}/_{210}$ .95%	$^{1}/_{219}$ .46%	$^{3}/_{435}$ .69%	$^{6}/_{864}$ .69%
47 - 56	$^{11}/_{371}$ 2.96%	$^{0}/_{322}$ 0	$^{9}/_{759}$ 1.18%	$^{20}/_{1461}$ 1.37%
37 - 46	$^{6}/_{520}$ 1.15%	$^{3}/_{402}$ .75%	$^{7}/_{670}$ 1.04%	$^{16}/_{1592}$ 1.01%
< 37	$^{5}/_{306}$ 1.63%	$^{2}/_{535}$ .37%	$^{1}/_{727}$ .14%	$^{8}/_{1568}$ .51%
	$^{24}/_{1407}$ 1.71%	$^{6}/_{1478}$ .41%	$^{20}/_{2591}$ .77%	

$X^2 = 14.9$ $P < .001$

Note: 4 - 9 years in one speciality and under 37, high risk to anaesthetists.

Anaesthetists $^{5}/_{265}$ 1.89% Other Hospital $^{2}/_{469}$ 0.43% Non-Hospital $^{0}/_{701}$ 0%

TABLE 35 Cardiovascular Disease

	Number	% of Cardiovascular Diseases
Infarction	78	36.4%
Hypertension	54	25.2%
Angina/I.H.D.	27	12.6%
Arrhythmia	18	8.4%
Myocarditis/Pericarditis	14	6.5%
Strokes/Subarachnoid	9	4.2%
R.H.D./S.B.E.	9	4.2%
Peripheral Vasc. D./Aneurysm	5	2.3%

$^{214}/_{5476}$ (3.91%)

Notes: Infarction + Hypertension coded as 'Infarction.'

Hypertension + Stroke coded as 'Stroke'.

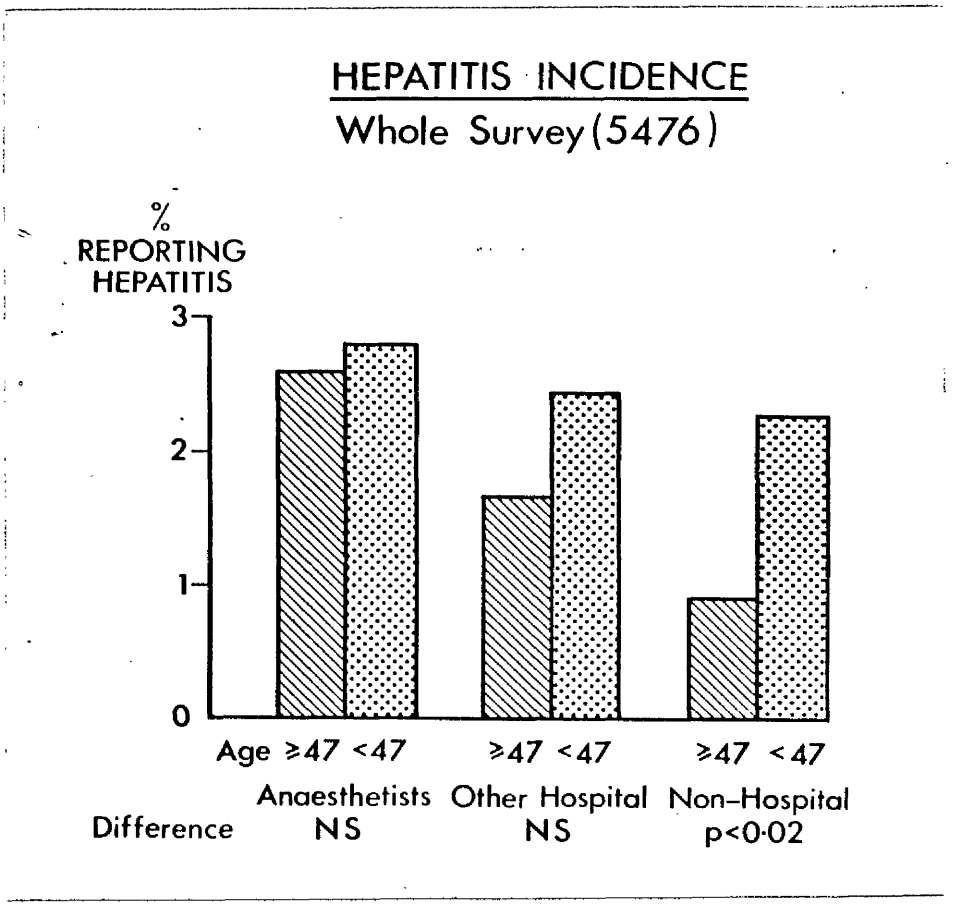


Figure 2. Frequency of hepatitis (%) in male doctors. Three occupational groups. Reports of illness in the previous ten years (1963-72) only are included.

myocardial infarction and arterial hypertension, although 18 respondents complained of troublesome cardiac arrhythmia without there being an apparent diagnosis of myocardial ischaemia or infarction.

Table 36 shows that anaesthetists do not appear to be particularly susceptible to any of the disease categories with the possible exception of arterial hypertension. However, myocardial infarction was commoner in anaesthetists and non-hospital doctors than in other doctors who worked in hospital.

Table 37 shows the distribution of complaints of angina, infarction, hypertension or arrhythmia according to the occupational groups and age. The group worst affected was the doctors who did not work in hospital, although there was a significant difference between anaesthetists and other hospital workers.

Gastrointestinal Disease

Table 38 shows the distribution of various types of gastrointestinal disease among the respondents. The commonest complaint was peptic ulcer which was present in 1.3% of the total respondents.

Table 39 shows a further sub-division of these diseases in respect of the occupational groups. The anaesthetists had a significantly higher frequency of peptic ulcer and gall bladder disease compared with the other 2 occupational categories.

DISCUSSION

The results of this part of the enquiry cannot be regarded as conclusive evidence as to the frequency of diseases in the male responders other/...

TABLE 36 Cardiovascular disease and speciality

	Angina/IHD	Infarction	Hypertension	Arrhythmias	Periph. VD	Strokes	RHD/SBE	Myocarditis
Anaesthetists	8/1407 .56%	20 1.42%	22 1.6%	8 .6%	1 .07%	4 .28%	2 .14%	6 .43%
Other Hospital	7/1478 .47%	13 .88%	11 .74%	1 .07%	1 .07%	1 .07%	2 .14%	1 .07%
Non-Hospital	12/2591 .46%	45 1.7%	21 .81%	9 .34%	3 .11%	4 .15%	5 .19%	7 .27%
X^2		10.3	6.5	5.62				3.7
P		<.01	<0.5	<.1				N.S.

TABLE 10 Angina, Infarctions, Hypertensions and Arrhythmias. All doctors.

Age	Anaesthetists		Other Hospital		Non-Hospital		Total
57 - 66	21	10.0%	16	7.3%	38	8.7%	$^{75}/_{864}$ 8.7%
47 - 56	31	8.4%	12	3.7%	40	5.3%	$^{83}/_{1461}$ 5.7%
37 - 46	6	1.16%	4	1.0%	8	1.2%	$^{18}/_{1592}$ 1.1%
< 37	0	0%	0	0%	1	.14%	$^{1}/_{1568}$ .06%
	58	3.36%	32	2.17%	87	4.19%	

$X^2 = 9.07$ $0.02 > P > 0.01$

TABLE 38 Gastrointestinal disease. All respondents.

	Cases	% of 5476
Peptic Ulcer	75	1.37
Gall Bladder	42	.77
Diverticular Disease	20	.36
Ulc Colitis/Crohn's Disease	13	.24
Appendicitis	13	.24
Cancers	11	.2
Coeliac Disease	8	.15
Pancreatic Disease	6	.11
Irritable colon	4	.07
Miscellaneous	21	.38
	213	3.9

TABLE 39 Gastrointestinal disease in three occupational groups.
Numbers in each category and % of group.

	G.I. Cancer	%	Peptic Ulcer		Gall Bladder		Diverticular Disease		U. Colitis Crohn's		Appendix		Misc.	
Anaesthetists (1407)	3	.21	29	2.06	16	1.14	3	.21	5	.36	3	.21	12	.85
Hospital (1478)	2	.13	14	.95	11	.74	2	.13	3	.2	3	.2	8	.5
Non-Hospital (2591)	6	.23	32	1.24	15	.58	15	.58	5	.19	7	.27	19	.73

X^2 = 7.53 3.75

0.05>P>0.02 0.2>P>.1

than in the case of cancer, liver disease and kidney disease since the questionnaire did not contain specific questions relating to the wide range of problems which were reported to us. The reasons for asking about cancer, liver disease and kidney disease have been summarised in Chapter 1. Corbett and others (1973) have shown an increase in the incidence of cancer in nurse anaesthetists in the State of Michigan and claim that this finding may be attributable to operating theatre exposure. It is reassuring to find that in the United Kingdom male anaesthetists do not appear to be specially at risk from this problem, although there is no data from the United Kingdom about female anaesthetists and it is worth noting that Cohen et al (1974), in the United States Ad Hoc Committee study, found an increase in cancer in women respondents. Clearly, this is a matter which should be kept under review.

The increase in the reporting of liver disease by anaesthetists, particularly hepatitis, must give rise to concern. Any attempt at forming an association between these findings and operating theatre pollution would focus on halothane as a possible hepatotoxic agent. Since the report of Klatskin and Kimberg (1969), there have been recurring suggestions that anaesthetists may be at risk from the effects of halothane. Although this agent has been shown to be hepatotoxic in animals (Stevens et al, 1975) and in man (Trowell, Peto and Crampton Smith, 1975; Wright et al, 1975), it seems much more likely that the findings reported here are a result of viral infection (Waterson, 1976, in press).

Anxiety about renal damage associated with anaesthetic employment is a problem confined to the United States. These fears are based on the demonstrable nephrotoxicity of methoxyflurane (Mazze, Trudell and /...

Cousins, 1971). In this context, it is interesting to note that in the U.S. enquiry (Cohen et al, 1974) both anaesthetists and non-anaesthetists were found to have an increased frequency of renal disease compared with their British counterparts. However, this difference was largely explained on the basis of renal lithiasis (Chapter 5). Methoxyflurane is not employed commonly in the United Kingdom and consequently there is little anxiety about renal disease in anaesthetists in this country.

It is the author's opinion that some credence should be given to the reporting of back troubles by anaesthetists. In the present survey, these complaints were entered only when there appeared to be some evidence of serious incapacity or major surgery or both. The difference between anaesthetists and non-anaesthetists in this respect could be explained by the frequent involvement of the anaesthetists in lifting patients from the trolley to the operating table or vice versa. However, such a claim is compromised by the finding that the frequency of such problems in both anaesthetists and control subjects in the United States was approximately the same as that in the British anaesthetists. Indeed, it is the British control subjects who seem to have the abnormally low frequency of such complaints.

The findings in relation to arterial hypertension and peptic ulcer are difficult to interpret. Clearly, both conditions may be subject to considerable bias in reporting. Moreover, the frequency of both complaints in all groups in this study is less than that which has been reported for hypertension (Hawthorne, Greaves and Beevers, 1974) or peptic ulcer (Hodgkin et al, 1970; Doll, Avery, Jones and Buckatzsh, 1951; Cotton, 1973).

It seems reasonable to suggest that the problem of hepatitis in /...

anaesthetists should be kept under surveillance by prospective survey in which the details of the diagnosis could be documented, but there are no obvious pointers in the rest of the data presented in this chapter which suggest that anaesthetists are specially at risk from other diseases.

CHAPTER 5 COMPARISON OF U.K. AND U.S. DATA

Confidence in the conclusions from health studies of the type reported in this thesis is greatly enhanced by the demonstration of similar findings in other similar populations. A preliminary comparison of the data from the two British surveys (Chapters 2, 3 and 4) and the report of the U.S. Ad Hoc Committee (Cohen et al, 1974) suggested that there was a measure of agreement between them sufficient to warrant a more detailed analysis which would allow the closest possible comparison.

Through the generosity of the University of Stanford, California, and the National Institute for Occupational Safety and Health, the author had the opportunity to spend a short period of time with Dr. Ellis Cohen, who was the instigator of the American enquiry, and his team. This chapter is a summary of the findings in this joint exercise.

The three surveys

The U.K. surveys have been described previously (Chapters 2 and 3):

(1) A survey of 1034 female anaesthetists and 1330 controls. Reply rate 82.1% and 80.0%.

(2) A survey of 7949 male doctors including most of the male anaesthetists in the U.K. Reply rate 70.1%.

The U.S. survey was of 49,585 exposed* operating theatre personnel in four professional societies (physicians, anesthetists, nurse anesthetists, operating room nurses, and operating room technicians), and 23,911 controls (not exposed) in two professional societies (paediatric physicians and a sample of the membership of the American Nurses Association).

---

* that is working in a contaminated operating theatre environment.

The U.S. survey form is shown in Appendix J.

Table 40 shows the numbers of physicians in the various groups in the three surveys and the respective reply rates. There are no British data to correspond with the American survey of non-medical personnel.

Female surveys

In the original U.S. publication (Cohen et al, 1974) data for female anaesthetists were included only if the respondent had worked in anaesthesia for a period of not less than one year before the onset of the pregnancy. In the combined analysis of replies from female doctors, less stringent criteria were applied. Thus, the U.K. data relate to respondents working in an operating theatre at the beginning of the pregnancy irrespective of the previous work history and similar criteria have been applied to the U.S. data.

The female surveys differ in that the U.S. data was collected in 1973 and refers to pregnancies in the period 1962 to 1972 only whereas the U.K. data was collected in 1971 and includes all pregnancies reported by the respondents. The maternal age was not available in the U.K. survey so that age standardisation could not be performed.

Male surveys

In the original U.K. survey of male physicians, all the respondents who worked in an operating theatre were regarded as a single 'exposed' group. In the present combined analysis, the U.K. test group comprises doctors who were working as anaesthetists in 1972, data from non-anaesthetists who worked in the operating theatre having been discarded. Additional differences between the U.K. male data in the joint analysis and in /...

TABLE 40 TOTAL MAILINGS AND REPLIES

	United Kingdom		United States	
	Total Mailings	Responses	Total Mailings	Responses
Males:				
Anaesthetists	1901	1407 (74.0%)	9793	6558 (73.7%)
Paediatricians	-	-	7024	2893 (45.0%)
Non-anaesthetist physicians	6048	4100 (67.8%)	-	-
Females:				
Anaesthetists	1034	849 (82.0%)	1399	1059 (82.0%)
Paediatricians	-	-	966	639 (79.4%)
Non-anaesthetist physicians	1330	1064 (80.0%)	-	-

Chapter 3 are that the obstetric data in this chapter relate to events in the 10 year period 1962-1972 only and the definition of spontaneous abortion has been changed from a gestation period of 28 weeks or less to one of 20 weeks or less. This altered definition conforms to the standard accepted within the United States.

The obstetric data analysis for male respondents in the two countries are similar in that all data were collected during 1973 and relate to events in the period 1962-1972; each test group comprises anaesthetists exclusively; each control group comprises physicians who have not worked in the operating theatre; the criterion for entry as an anaesthetist is that the respondent was working in anaesthesia at the beginning of his wife's pregnancy irrespective of previous work history; and the criterion for spontaneous abortion was a gestation period of 20 weeks or less.

The male survey data from the two countries differ in that the U.K. control group consists of several groups of physician specialists not employed in the operating room, while the U.S. control group was taken from one specialty (paediatrics) exclusively.

The return rates quoted in the original U.S. study (Cohen et al, 1974) were calculated differently from those shown in ~~Chapters 2 and 3~~ that publication, to allow for the fact that questionnaires which were returned by the postal services (addressee unknown) should be deducted from the total numbers who were presumed to have received the questionnaire and in relation to whom the response rates of the British studies were calculated.

RESULTS

Female Respondents

The adjusted rates varied from 42% for U.S. male paediatricians to 82% for female anaesthetists in the U.S. and the U.K. Table 41 shows that the mean age, at the time of the survey, of the female respondents in the U.S. (41.6 yr) was greater than in the U.K. (39.3 yr). Similar differences occur in the control groups: U.S. 47.2 yr and U.K. 41.8 yr. All rates for the U.S. respondents were age standardised to the same standard population (Cohen et al, 1974). In fact, the effect of this procedure on the actual rates is extremely small.

The adjusted number of pregnancies in the U.S. study was 949 of which 549 were in anaesthetics. The corresponding values for the U.K. were 2,887 and 737.

Spontaneous Abortion

The rate for spontaneous miscarriage averaged 17.1 per 100 pregnancies for exposed female anaesthetists in the U.S. compared with 8.9 for female paediatricians ($P < 0.01$). In the U.K., the rate for female anaesthetists was 17.5% compared with 13.9% for non-anaesthetist physicians ($X^2 = 5.2$; $P < 0.05$). Though not shown in Table 41, it was found that among non-working anaesthetists the rate was 15.7% in the U.S. and 13.7% in the U.K. Both values were lower than the corresponding values for working anaesthetists but the differences were not significant ($P = 0.35$ [U.S.]; $P < 0.2$ [U.K.]). "Not working" was defined in the U.S. study as the absence of operating theatre exposure for at least one year before the pregnancy and in the first trimester. In the U.K. study, it was defined as absence from the operating theatre at the onset of the pregnancy and during the first trimester.

TABLE 41 Adjusted data from combined surveys of female physicians in the U.K. and U.S. Rates are per 100. Skin abnormalities are excluded from congenital abnormalities. See text for further details.

	Exposed Anaesthetists			Control Doctors			Significance for combined data
	United States	United Kingdom	Combined	United States	United Kingdom	Combined	
Age (yr)	41.6	39.3		47.2	41.8		
Pregnancies	596	737	1333	355		2505	
Abortions/ total pregnancies (%)	15.7	17.5	16.7	9.6	13.95	13.3	$P < 0.001$
Liveborn children	494	599	1093	313	1817	2130	
Congenital abnormalities/ liveborn children (%)	5.5	5.5	5.5	2.8	4.2	4.0	$P < 0.1$

Table 41 shows also rates for spontaneous abortion obtained by pooling the data from the female anaesthetists and the control subjects in both countries. The combined rate for anaesthetists is 16.7% compared with 13.3% in the control group ($P < 0.001$).

Congenital Abnormalities

In the previous report of the U.S. survey (Cohen et al, 1974), congenital abnormalities of the skin were excluded from the reported rate of congenital abnormalities (5.9% for female anaesthetists and 3.0% for female paediatricians [$P = 0.07$]). The adjusted U.K. rate was 5.5% for anaesthetists and 4.2% for the controls ($X^2 = 1.5$, $P<0.03$). For non-working female anaesthetists, the rate was 3.4% in the U.S. and 2.1% in the U.K. The U.K. value was significantly different from the control ($X^2 = 4.5$, $P < 0.05$). Combining the U.S. and U.K. data gives a rate for exposed female anaesthetists of 5.5% (983 live births) and 2.5% (400 live births) for the non-working anaesthetists. ($X^2 = 5.7$; $P < 0.02$). The combined control value was 4.0% ($X^2 = 1.25$; $P < 0.01$).

In the original U.S. study, attention was drawn to a significant difference between anaesthetists and controls in respect of multifactorial congenital abnormalities (including abnormalities of the hips, club foot, cleft palate and lip, spina bifida, hydrocephalus, atrial septal defect, patent ductus arteriosus, pyloric stenosis). The frequency in the U.S., from the adjusted data, was 1.2% in anaesthetists and 0.2% in the controls ($P = 0.06$). In the U.K., the respective values were 0.7% and 1.1% ($P=0.80$).

Male Respondents

Table 42 shows an arrangement, similar to that in Table 41, of the /...

TABLE 42 Adjusted data from combined surveys of male physicians in the U.S. and U.K.
Rates are per 100. Skin abnormalities are excluded from congenital abnormalities.

	Exposed Anaesthetists			Control Physicians			Significance* for combined data
	United States	United* Kingdom	Combined	United States	United* Kingdom	Combined	
Father's age (yr)	45.2	39.0		51.8	40.8		
Pregnancies	4143	1382	5525	2261	2493	4754	
Miscarriages/ Pregnancies (%)	12.1	13.4**	12.4	12.0	11.5**	11.7	$P > 0.2$
Liveborn children	3597	1180	4777	1970	2174	4144	
Congenital abnormalities/ Liveborn children (%)	5.3	4.2***	5.0	3.9	3.6***	3.7	$P < 0.001$

* Surgeons, radiologists and incidental exposure excluded. Pregnancies before 1962 excluded also.
** Comparison of the U.K. exposed and unexposed data gives $X^2 = 2.9$; $P < 0.1$
*** Comparison of the U.K. exposed and unexposed data gives $X^2 = 0.7$; P = N.S.

replies from male anaesthetists. The mean age of male anaesthetists at the time of the study was less in the U.K. (36.1 yr) than in the U.S. (45.2 yr). The mean age of the U.S. control group was 51.8 yr and that of the U.K. control group was 37.1 yr. Excluding therapeutic abortions and adjusting for maternal age, there were 4,143 pregnancies in the wives of exposed male anaesthetists in the United States and 2,261 in the wives of the controls. In the U.K. study (excluding therapeutic abortions) there were 1,382 pregnancies in the wives of male anaesthetists and 2,493 in the wives of the controls.

Spontaneous Abortion

The previously reported rate was 11.6% in the wives of male anaesthetists in the U.S. and 12.6% for the controls. The difference is not statistically significant (Cohen et al, 1974). In the U.K. study (Chapter 3), the rate was 11.1% in the wives of exposed male anaesthetists and other operating theatre workers, and 10.9% in the wives of non-exposed doctors.

Pooling the data from male respondents in the two countries (Table 43) gives a combined rate for spontaneous abortion of 12.4% for anaesthetists and 11.7% for the controls ($P > 0.2$).

Congenital Abnormalities

The previously reported congenital abnormality rate (skin excluded) was 5.4% for the wives of anaesthetists in the U.S. and 4.2% for the controls ($P = 0.04$). In the U.K., the rate for wives of male anaesthetists was 4.2% (skin excluded) and 3.6% for the controls. The difference was not statistically significant.

In pooling the data for the two countries, the combined rate for anaesthetists is 5.0% and 3.7% for the controls. This difference is statistically significant ($P < 0.001$).

The frequency of multifactorial congenital abnormalities was 1.6% for the wives of anaesthetists and 0.9% for the controls in the U.S. ($P = 0.03$). In the U.K., the frequency was 1.02% for the wives of anaesthetists and 0.83% for the controls. The pooled data give a rate of 1.45 for the wives of anaesthetists and 0.88 for the wives of controls.

Other Diseases

Table 43 shows the data of the U.K. male study and the males in the U.S. study which relate to other major diseases of the respondents themselves. The British data have been adjusted for age as described by Cohen et al (1974). Thus, there are small differences between the rates reported for the U.K. respondents in Table 4 and those reported in Chapter 4.

The frequency of cancer in the U.S. was 0.7 per 100 respondents in both male anaesthetists and male paediatricians. The corresponding rates in the U.K. were 1.1% and 0.8%. There is no statistically significant difference between either anaesthetists and controls or between doctors in the two countries. The rate for liver disease (serum hepatitis included) in the U.S. was 4.3% for anaesthetists and 2.5% for paediatricians ($P < 0.01$). In the U.K., the rates were 3.8% and 2.3% ($P < 0.01$). The kidney disease rate was 4.2% for anaesthetists in the U.S. and 4.6% for the controls. In the U.K., the rates were 1.7% and 2.1%. Although there is no difference between anaesthetists and controls in either country, /...

TABLE 43 Disease rates per 100 for male anaesthetists and non-anaesthetist controls in the U.K. and U.S. The controls were male paediatricians (U.S.) and doctors in all branches of medicine other than those involving operating theatre work (U.K.)

	United Kingdom		United States	
	Anaesthetists	Controls	Anaesthetists	Controls
Cancer (skin excluded)	1.1	0.8	0.7	0.7
Laukaemia	0.24	0.24	0.08	0.03
Liver disease	3.8 *	2.3 *	4.3 *	2.5 *
Kidney disease	1.7	2.1	4.2	4.6
Lithiasis	1.3	1.1	3.1	3.3
Other diseases:				
Peptic ulcer	2.3 *	1.2 *	1.9	1.7
Gall bladder	1.3 *	0.5 *	0.9	1.0
Myoc. infarct.	1.7	1.8	1.7	1.6
A. hypertension	1.8 *	0.8 *	2.3	2.5
Lumbar disc	1.4 *	0.5 *	1.3	1.5
Ulc. colitis	0.3	0.2	0.24 **	0.08 **

* $P < 0.01$ ** $P = 0.03$

the difference between the American doctors and the British doctors is highly significant ($P < 0.01$). Part of the explanation for this difference is an increased reporting of renal lithiasis by the Americans.

The frequency of peptic ulcer, gall bladder disease, arterial hypertension, and serious lumbar spine disease was significantly greater in the anaesthetists in the U.K. compared with the controls. However, such differences were not found in the U.S. study. On the other hand, in that study, the rates for ulcerative colitis were significantly different.

DISCUSSION

This combined analysis greatly strengthens the findings of the two United Kingdom studies that women who are exposed in an operating theatre in the early part of a pregnancy have an increased risk of spontaneous abortion. It is clear also that such a risk does not apply to situations in which the father has worked in an operating theatre during the period of conception. It is of interest that combining the data does not show a significant effect on the rate of congenital abnormality as a result of female exposure, although there is a clear increase associated with male exposure.

The combined analysis confirms also the findings in the U.K. study that the practice of anaesthesia is not associated with a significant increase in the frequency of cancer or leukaemia but that liver disease, most commonly hepatitis, is an increased risk for the anaesthetist. The increased reporting of peptic ulcer, gall bladder disease and arterial hypertension in the British study was not confirmed in the American study. Similarly, the increased frequency of serious lumbar disc problems in British anaesthetists was not reflected in the American data. On the /...

one hand, it might be expected that American anaesthetists would be less liable to back problems since the normal practice in transferring patients within the operating theatre is different in the United States, where the theatres tend to be well staffed with porters and where it is unusual for the traditional stretcher to be used in transferring patients from the operating table to the trolley. On the other hand, the rate for such problems in the U.S. study, in both the anaesthetist and control groups, is closer to the rate for the U.K. anaesthetists than to the U.K. control group. There is no obvious explanation for this.

CHAPTER 6 CONCLUSIONS, RECOMMENDATIONS AND FURTHER INVESTIGATION

Health Hazards

The data presented in Chapters 2 and 3 and the data from the United States (Cohen, Bellsville and Brown, 1971; Cohen et al, 1974) are strong evidence that the practice of anaesthesia or operating theatre exposure, or both, by pregnant women increases the risk of spontaneous abortion. The marked increase in the frequency of involuntary infertility in women anaesthetists compared with the control group (Chapter 2) remains to be confirmed. There must continue to be anxiety about an association between anaesthetic practice and congenital abnormality, although the evidence is less clear than is that relating to spontaneous abortion.

Operating Theatre Contamination

There is no direct evidence to link these findings of obstetric hazard with operating theatre contamination by anaesthetics. It follows, therefore, that the assumption that halothane is a specially harmful pollutant (Vaughn, Mapleson and Mushin, 1973) may be misleading.

In spite of these observations, there is now a widespread demand for measures to reduce or prevent operating theatre contamination. At the beginning of 1975, the Association of Anaesthetists of Great Britain and Ireland and the Department of Health formed a joint working party, of which the author was a member, to deal with the problem. A preliminary statement has been published (Vickers, 1975) and recommends that consideration be given to the installation of either passive or active scavenging systems where possible. The various methods of /...

scavenging have been reviewed by Parbrook and Monk (1975) and a suitable system may be expected to reduce the average level of contamination by a factor of 10.

Within the last year, some anaesthetists have advocated a return to closed circuit anaesthesia as a method of reducing contamination of the theatre air but Barton and Nunn (1975) have highlighted the relative complexity of such a solution. It would be unfortunate if patients were to incur real risks from misuse of complex systems as a result of attempts to obviate an assumed risk of theatre pollution.

There are many safeguards within the scope of individual anaesthetists, and others, which are worthy of attention, such as the filling of vaporizers in the evening in preference to the morning (Parbrook and Monk, 1975), the avoidance of anaesthetics as cleansing agents and the careless discharge of anaesthetic gases from anaesthetic machines after the circuitry has been disconnected from the patient.

It may be that the current anxiety will stimulate the development of non-gaseous anaesthetics.

Future Action

Although anti-contamination measures would seem to be appropriate in the light of uncertainty as to the cause of the increased morbidity in women anaesthetists, it would be foolish to assume that effective measures will bring an end to the problem. Thus, prospective studies should be undertaken to monitor the health of women who work in operating theatres.

It is hoped that such an inquiry in the U.K. will be commenced /...

by the author in the Spring of 1976. Its purpose is to survey annually for 5 years:

1. To determine by prospective survey whether -

   (a) there continues to be an apparent increase in the frequency of spontaneous abortion in women medical practitioners who work in operating theatres.

   (b) the frequency of spontaneous abortion in married women nurses who work in operating theatres is different from that of nurses who do not work in operating theatres.

2. To determine in both female doctors and female nurses whether working in an operating theatre is associated with any other adverse effects on child bearing, such as involuntary infertility, or congenital abnormality of liveborn children.

3. To seek information regarding the general health of the women surveyed with special reference to the reported increase in the frequency of malignant disease in women who work in operating theatres.

Plan of Investigation

Controlled Prospective 5 Year Survey of Women Anaesthetists

Determination of numbers to be studied:

The following table (based on the Department of Health data, June 1975) shows the number of women in the hospital specialties grouped according to age -

/...

Age (yr)	England & Wales	(%)	Scotland*	Total
less than 30	1842	40	184	2026
30 - 34	805	18	80	885
35 - 39	552	12	55	607
more than 40	1378	30	138	2516
total age known	4577	-	-	-
total	4590	100	459	5049

(* Assume 10% of England & Wales figure)

Total number of women in specialties at SHO level or above (from DHSS tables) = 4244

Assume difference (5049 - 4244) should be deducted from "less than 30" group (i.e. SHO etc.) (805)

Therefore we should survey all women aged 39 or less in the grades of SHO and above = 2713

The result of our previous surveys suggest that 66% of all hospital specialist women are married but we think it reasonable to assume 75% for the "39 or less" group = 2035

Approximately 1 of 5 hospital women at the grades of SHO or above is in anaesthesia. Thus, we would hope to commence the survey with 407 married women anaesthetists and 1628 married women controls.

Over a five year period, we expect these numbers to increase:

annual gain (1/5* of "less than 30" SHO and above)	244
losses (1/5 of "35-39" group on age criteria)	121
nett gain per annum	123
nett gain over 5 years	492

cumulative total in survey over five years (2035 + 492) = 2527

(anaesthetists 505)

(controls 2022)

In order to have the same number of pregnancies as was analysed in our 1972 retrospective survey (anaesthetists 1073; controls 2150), we would be hoping for as much as two pregnancies for each anaesthetist over the five year period. Since this is unlikely, there exists the possibility that even after five years the numbers would be insufficient for analysis. On the other hand, a clear difference in the frequency of spontaneous abortion, associated with operating room exposure, was obtained as a result of matching of data in our second study (1975) with as little as 386 and 435 exposed pregnancies in the different groups. Thus, the control group should be as large as possible and we propose to include all women in hospital medicine as indicated.

It is proposed also to plan a parallel study of female nurses.

Advice to Theatre Staff

What advice is to be given to the anaesthetist or nurse who wishes to work in an operating theatre when either attempting to become pregnant, or when pregnant? In the present uncertainty, it is reasonable to explain the known facts and to co-operate sympathetically with the woman's own wishes. Thus, the author does not feel that a sufficient case exists for excluding such persons from the operating theatre. On the other hand, a woman who has suffered a previous abortion while working, or an older woman having a first pregnancy, would be wise to cease operating theatre work. Clearly, it would be of interest to know whether previous operating theatre work influences a pregnancy even if the mother has ceased work before conception. None of the British data allowed examination of this factor. The design of the U.S. enquiry (Cohen et al, 1974) did allow such an analysis but, unhappily, a clear conclusion could not be made.

REFERENCES

Agostino, D. and Cliffton, E.E. (1964) Anaesthetic effect on pulmonary metastases in rats. Archives of Surgery, 88, 735.

Aldrete, J.A. and Virtue, R.W. (1967) Effects of prolonged inhalation of hydrocarbon gases on rats. Anesthesiology, 28, 238.

Andersen, N.B. (1966) The effects of CNS depressants on cell mitosis. Acta Anaesthesiologica Scandinavica, Suppl. 22.

Andersen, N.B. (1968) The teratogenicity of cyclopropane in the chicken. Anesthesiology, 29, 113.

Askrog, V.F. (1970) Expiratory valve with gas collecting canal. Nordisk Medicin, 83, 811.

Askrog, V.F. and Harvald, B. (1970) Teratogen effect of inhalations anaestetika. Nordisk Medicin, 83, 498.

Askrog, V.F. and Harvald, B. (1970) Resultaer af genetiske undersøgilser orer dansk anaestisi personel. Nordisk Medecin, 83, 177.

Barton, F. and Nunn, J.F. (1975) Totally closed circuit nitrous oxide/oxygen anaesthesia. British Journal of Anaesthesia, 47, 350.

Basford, A.B. and Fink, B.R. (1968) The teratogenicity of halothane in the rat. Anesthesiology, 29, 1167.

Bruce, D.L., Bach, M.J. and Arbit, J. (1974) Trace anaesthetic effects on percephral cognitive and motor skills. Anesthesiology, 40, 453.

Bruce, D.L., Eide, K.A., Linde, H.W. and Eckenhoff, J.E. (1968) Causes of death among anesthesiologists: a 20 year survey. Anesthesiology, 29, 565.

Bruce, D.L., Eide, K.A., Smith, N.J., Seltzer, F. and Dykes, M.H.M. (1974) A prospective survey of anesthesiologist mortality 1967-1971. Anesthesiology, 41, 71.

Bruce, D.L. and Taurig, H.N. (1969) The effect of halothane on the cell cycle in rat small intestine. Anesthesiology, 30, 401.

Bruce, D.L. and Wingard, D.W. (1971) Anesthesia and the immune response. Anesthesiology, 34, 271.

Buinauskas, P., McDonald, G.O. and Cole, W.H. (1958) Role of operative stress on the resistance of the experimental animal to inoculated cancer cells. Annals of Surgery, 148, 642.

Bullough, W.S. (1969) The chalones, Science Journal, 5, 71.

Butler, N.R. and Alberman, E.D. (1969) "Perinatal Problems" The second report of the 1958 British Perinatal Mortality Survey. London: E & S Livingstone, p. 363.

Carr, D.H. (1973) Anesthetic-induced abortion. Anesthesiology, 35, 335.

Cascorbi, H.F., Blake, D.A. and Helrich, M. (1970) Differences in the biotransformation of halothane in man. Anesthesiology, 32, 119.

Cohen, E.N. (1971) Metabolism of the volatile anesthetics. Anesthesiology, 40, 385.

Cohen, E.N., Bellville, J.W. and Brown, B.W. (1971) Anesthesia, pregnancy, and miscarriage. A study of operating room nurses and anesthetists. Anesthesiology, 35, 343.

Cohen, E.N., Brown, B.W., Bruce, D.L., Cascorbi, H.F., Corbett, T.H., Jones, T.W., Whitcher, C.E. (1974) Occupational disease among operating room personnel: a national study. Anesthesiology, 41, 321.

Corbett, T.H. and Ball, G.L. (1971) Chronic exposure to methoxyflurane: a possible occupational hazard to anesthesiologists. Anesthesiology, 34, 532.

Corbett, T.H., Cornell, R.G. and Endres, J.L. (1973) Effects of low concentrations of nitrous oxide on rat pregnancy. Anesthesiology, 39, 473.

Corbett, T.H., Cornell, R.G., Lieding, K. and Endres, J.L. (1973) Incidence of cancer among Michigan nurse-anesthetists. Anesthesiology, 38, 260.

Cotton, P.B. (1973) 1/100 of opoulation investigated each year for symptoms of P.U. British Medical Journal, 2, 61.

Crocker, W. and Knight, L.I. (1908) Effect of illuminating gas and /...

ethylene upon flowering carnations. Botanical Gazette, 46, 259.

Cullen, B.F., and Sundsmo (1974) Failure of halothane anesthesia to alter growth of sarcoma in mice. Anesthesiology, 41, 580.

Davie, R., Butler, N. and Goldstein, H. (1972) From birth to seven. The second report of the National Child Development Study (1958 Cohort).

Doll, R., Avery Jones, F., Buckatzsh, M.M. (1951) 30% of adult population over a 5 year period complaining of dyspepsia. Medical Research Council Special Reports, Series No. 276. London : H.M.S.O.

Doll, R. and Hill, A.B. (1954) The mortality of doctors in relation to their smoking habits. British Medical Journal, 1, 1451.

Doll, R. and Hill, A.B. (1964) Mortality in relation to smoking. 10 years' observations of British doctors. British Medical Journal, 1, 1399.

Dollery, C.T. (1972) Enzyme induction. British Journal of Anaesthesia, 44, 961.

Eastwood, D.W., Green, C.D., Lambdin, M.A. and Gardner, R. (1963) Effect of nitrous oxide on the white cell count in leukaemia. New England Journal of Medicine, 268, 297.

Editorial (1971)(a) A personal risk. British Journal of Anaesthesia, 43, 419.

Editorial (1972)(b) Anaesthesia, Pregnancy and Pollution. British Journal of Anaesthesia, 44, 541.

Editorial (1972) [c] Harmful pollution by anaesthetic gases? The Lancet, 2, 519.

Editorial (1975) Dangers in Radiology. British Medical Journal, 3, 396.

Eger, E.I. ii (1971) Inhalational Anaesthesia: Pharmacokinetics. in General Anaesthesia, Vol. 1, Eds: Gray, T.C. and Nunn, J.F. London : Butterworths.

Ferguson-Smith, M.A. (1969) Notes on chromosomal abnormalities in obstetrics. Practical Obstetric Problems. Ed: Donald, I. London: Lloyd-Luke

Fink, B.R. (1966) Carcinostatic action of nitrous oxide in mice. Anesthesiology, 27, 214.

Fink, B.R. (1971) Effect of anaesthesia on cell division. General Anaesthesia, Vol. 1. Eds: Gray, T.C. and Nunn, J.F. London: Butterworths.

Fink, B.R., Shepard, T.H. and Blandau, R.J. (1967) Teratogenic activity of nitrous oxide. Nature (London) 214, 146.

Fischer, B. and Fischer, E.R. (1959) Effect of surgical trauma on growth of experimentally induced hepatic metastases. Annals of Surgery, 150, 731.

Gatti, R.A. and Good, R.A. (1970) Aging immunity and malignancy. Geriatrics, 25, 158.

Gaylord, H.R. and Simpson, B.T. (1916) The effect of certain anaesthetics and blood loss upon the growth of transplanted mouse cancer. Journal of Cancer Research, 1, 379.

Hallen, B., Ehrner-Samuel, H. and Thomason, M. (1970) Measurements of halothane in the atmosphere of air operating theatre and in expired air and blood of personnel during routine anaesthetic work. Acta Anaesthesiologica Scandinavica, 14, 70.

Hawthorne, V.M., Greaves, D.A. and Beevers, D.G. (1974) Blood pressure in a Scottish town. British Medical Journal, 3, 600.

Hertig, A.T. and Rock, J. (1949) Abortion associated with foetal abnormality. American Journal of Obstetrics and Gynaecology, 38, 968.

Hewer, C.L. (1972) Occupational hazards of the anaesthetist. Recent Advances in Anaesthesia dna Analgesia. Ed: Hewer, C.L. London: Churchill Livingstone, Chapter 9.

Hodgkin, G.K.H., Freedman, R., Fuller, I. and Whewell, J. (1970) Duodenal ulcer and recurrent dyspepsia. British Medical Journal, 3, 368.

Javert, C.J. (1957) Spontaneous and habitual abortion. New York : McGraw-Hill, p. 209.

Kieler, J. (1957) Cytotoxic effect of nitrous oxide at different oxygen tensions. Acta Pharmacologica et Toxicologica, 13, 301.

Klatskin, G. and Kimberg, D.V. (1969) Recurrent hepatitis attributable to halothane sensitisation in an anesthetist. New England Medical Journal, 280, 515.

Knill-Jones, R.P., Moir, D.D., Rodrigues, L.V., and Spence, A.A. (1972) Anaesthetic practice and pregnancy. Controlled survey of women anaesthetists in the United Kingdom. The Lancet, 1, 1326.

Lassen, H.C.A., Henriksen, E., Neukirch, F. and Kristensen, H.S. (1956) Treatment of tetanus - severe bone marrow depression after prolonged nitrous oxide anaesthesia. The Lancet, 2, 527.

Linde, H.W. and Berman, M.L. (1971) Non-specific stimulation of drug metabolizing enzymes by inhalation anesthetic agents. Anesthesia and Analgesia (Cleveland), 50, 656.

Linde, H.W. and Bruce, D.L. (1969) Occupational exposure of anesthesiologists to halothane, N_2O and radiation. Anesthesiology, 30, 313.

Marresse, R.A. (1969) A safe method for discharging anesthetic gases. Anesthesiology, 31, 371.

Mazze, R.I., Trudell, J.R. and Cousins, M.J. (1971) Methoxyflurane metabolism and renal dysfunction: clinical correlation in man. Anesthesiology, 35, 247.

Nunn, J.F., Dixon, K.L. and Moore, J.R. (1968) Effect of halothane on tetrahymena pyriformis. British Journal of Anaesthesia, 40, 145.

Parbrook, G.D. (1969) Leucopaenic effect of prolonged nitrous oxide treatment. British Journal of Anaesthesia, 39, 119.

Parbrook, G.D. and Monk, I.B. (1975) An expired gas collection and disposal system. British Journal of Anaesthesia, 47, 1185.

Pfaffli, P., Nikki, P. and Ahlman, K. (1972) Concentrations of anaesthetic gases in recovery rooms. British Journal of Anaesthesia, 44, 230.

Rao, P.N. (1968) Mitotic synchrony in mammalian cells treated with nitrous oxide at high pressure. Science (Washington) 160, 774.

Rose, K.D. and Rosow, I. (1973) Physicians who kill themselves. Archives of General Psychiatry, 29, 800.

Roth, D.B. (1963) The frequency of spontaneous abortion. International Journal of Fertility, 8, 431.

Russell, C.S., Taylor, R. and Law, B.E. (1968) Smoking in pregnancy: maternal blood pressure, pregnancy outcome, baby weight and growth and other related factors. A prospective study. British Journal of Preventive and Social Medicine, 22, 119.

Salvini, M., Binaschi, S. and Riva, M. (1971) Evaluation of the psychophysiological functions in humans exposed to trichloroethylene. British Journal of Industrial Medicine, 28, 293.

Schatten, W.E. and Kramer, W.M. (1958) An experimental study of postoperative tumor metastasis. II Effects of anesthesia, operation and cortisone administration on growth of pulmonary metastases. Cancer, 11, 460.

Shnider, S.M. and Webster, G.M. (1965) Maternal and fetal hazards of surgery during pregnancy. American Journal of Obstetrics and Gynecology, 92, 891.

Schreiner, H.R. and Gregoire, R.C. (1963) The effect of nitrous oxide on cellular growth. Federation Proceedings, 22, 424.

Simpson, B.R., Strunin, L. and Walton, B. (1975) Halothane and jaundice. British Hournal of Hospital Medicine, 13, 433.

Smith, W.D.A. (1975) Pollution and the anaesthetist. Recent Advances in Anaesthesia and Analgesia (12th edition) Ed: C.L. Hewer. In press.

Smith, B.E., Gaub, M.L. and Learer, S.B. (1968) Teratogenic effects of diethylether in the chick embryo. Toxocity of Anesthetics. Ed: B.R. Fink. Baltimore: Williams Wilkins, p. 269.

Smith, B.E., Gaub, M.L. and Moya, F. (1965) Investigation into the teratogenic effects of anaesthetic agents: the fluorinated agents. Anesthesiology, 26, 260.

Snegireff, S.L., Cox, J.R. and Eastwood, D.W. (1968) The effect of /...

N_2O, cyclopropane or halothane on neural tube nitotic index, weight, mortality and growth anomaly rate in the developing chick embryo. Toxicity of Anesthetics. Ed: B.R. Fink. Baltimore: Williams Wilkins, p. 279.

Stevens, W.C., Eger, E.I., White, A., Halsey, M.J., Munger, W., Gibbens, R.D., Dolan, W. and Shargel, R. (1975) Comparative toxicities of halothane, isoflurane and diethyl ether at subanaesthetic concentrations in laboratory animals. Anesthesiology, 42, 408.

Strunin, L., Knights, K., Strunin, J.M. and Ward, M.E. (1975) General anaesthesia during early pregnancy. British Journal of Surgery, 62, 471.

Trevino, E. and Gines, S. (1961) Dissemination of cancer. Prevention and Therapy. Eds: Cole, W.H., McDonald, C.O. and Roberts, S.S. New York: Appleton - Century - Crofts, p. 262.

Trowell, J., Peto, R. and Crampton-Smith, A. (1975) Controlled trial of repeated halothane anaesthetics in patients with carcinoma of the uterine cervix treated with radium. The Lancet, 1, 821.

Vaisman, A.I. (1967) Work in operating theatres and its effects on the health of anesthesiologists. Eksperimenta Khirurgica Anesthesiologica, 12, 44.

Van Dyke, R.A. (1966) Metabolism of volatile anesthetics - III. Induction of nucroscanal dechlorinating and ether - clearing enzymes. Journal of Pharmacology and Experimental Therapeutics, 154, 364.

Van Dyke, R.A. and Chenaveth, M.B. (1965) Metabolism of volatile anesthetics. Anesthesiology, 26, 348.

Vaughn, R.S., Mapleson, W.W. and Mushin, W.W. (1973) Prevention of pollution of operating theatres with halothane vapour by absorption with activated charcoal. British Medical Journal, 1, 727.

Vickers, M.D. (1975) Association of Anaesthetists of Great Britain and Ireland : Advice to members from the Council. Pollution of Operating Theatres. Anaesthesia, 30, 697.

Warburton, D. and Fraser, F C. (1964) Spontaneous abortion risks in man : Data from reproductive histories collected in a medical genetics unit. American Journal of Human Genetics, 16, 1.

Waterson, A.P. (1976) Hepatitis B as a hazard in anaesthetic practice British Journal of Anaesthesia, 48, 000 (in press).

Whitcher, C.E., Cohen, E.N. and Trudell, J.R. (1971) Chronic exposure to anesthetic gases in the operating room. Anesthesiology, 35, 348.

Wood, M., O'Malley, K. and Stevenson, I.H. (1974) Drug metabolizing ability in operating theatre personnel. British Journal of Anaesthesia, 46, 726.

Wright, R., Chisholm, M., Lloyd, B., Edwards, J.C., Eade, O.L., Hawksley, M., Moles, T.M. and Gardner, M.J. (1975) Controlled prospective study of the effect on liver function of multiple exposures to halothane. The Lancet 1, 817.

Yeakel, A.E. (1970) A device for eliminating overflow anesthetic gases from anesthetizing local Anesthesiology, 32, 280.

Yerushalmy, J. (1971) The relationship of parent cigarette smoking to outcome of pregnancy. Implications as to the problem of inferring causation from observed associations. American Journal of Epidemiology, 93, 443.

UNIVERSITY OF GLASGOW

CONFIDENTIAL ENQUIRY INTO THE POSSIBLE EFFECTS

OF ANAESTHETIC PRACTICE ON PREGNANCY:

SURVEY OF WOMEN ANAESTHETISTS

It is most important that you return this questionnaire. The results will be inconclusive unless a high return rate is obtained.

Your name and address will be seen only by one of three doctors and all questionnaires will be destroyed at the conclusion of the survey. Any publications which result from this survey will not permit the identification of any individual.

If you are unmarried and have never been married, then you need answer questions 1 to 3 only.

If you are married, or have been married, please answer all the questions.

Please pay special attention to the wording of questions 7 and 12.

Please do not write anything within the boxes.

****

(1) Name (capital letters)

(2) Address (capital letters) ☐☐☐☐☐ 1-5

---

(3) Are you, or have you been married? Yes/No ☐ 6

(4) Age ..... years ☐☐ 7-8

(5) How long have you been (or were you)engaged in anaesthetic practice? Number of years in anaesthetic practice:

(a) Whole time ..... years ☐☐ 9-10

(b) Part time ..... years ☐☐ 11-12

(c) If part time, please estimate average number of hours per week ..... hours ☐☐ 13-14

(6) Are you currently employed as an anaesthetist?

(a) Whole time Yes/No ☐ 15

(b) Part time Yes/No ☐ 16

P.T.O.

(7) Please complete the following table for all pregnancies of AT LEAST 28 WEEKS DURATION. Enter them in chronological order. Twins should appear as two separate consecutive entries. Other multiple births should be entered likewise. If there are more than eight children, enter the first eight only.

Maturity at delivery (weeks)	Was the child born alive? (yes/no)	If born alive did the child die within 4 weeks? (yes/no)	Sex of child	Congenital abnormalities (please specify)	Were you in anaesthetic employment during the first trimester? (yes/no)	Were you in anaesthetic employment during the second trimester? (yes/no)	
1. ☐☐	☐	☐	☐	☐	☐	☐	17-24
2. ☐☐	☐	☐	☐	☐	☐	☐	25-32
3. ☐☐	☐	☐	☐	☐	☐	☐	33-40
4. ☐☐	☐	☐	☐	☐	☐	☐	41-48
5. ☐☐	☐	☐	☐	☐	☐	☐	49-56
6. ☐☐	☐	☐	☐	☐	☐	☐	57-64
7. ☐☐	☐	☐	☐	☐	☐	☐	65-72
8. ☐☐	☐	☐	☐	☐	☐	☐	73-80

(8) Have you had more than eight children? Yes/No ☐ 6

(9) How many twin pregnancies have been entered? ..... ☐ 7

(10) How many multiple pregnancies other than twins have been entered? ..... ☐ 8

(11) Had you been in anaesthetic practice before your first child was born?

Yes/No/does not apply ☐ 9

(12) Please complete the following table for all pregnancies which terminated spontaneously BEFORE THE 28TH WEEK OF GESTATION:-

	Maturity (weeks)	Were you in anaesthetic employment during the first trimester? (yes/no)	Were you in anaesthetic employment during the second trimester? (yes/no)	Other information (e.g. congenital abnormality or known cause for miscarriage)
10-14	1. ☐☐	☐	☐	☐
15-19	2. ☐☐	☐	☐	☐
20-24	3. ☐☐	☐	☐	☐
25-29	4. ☐☐	☐	☐	☐
30-34	5. ☐☐	☐	☐	☐
35-39	6. ☐☐	☐	☐	☐
40-44	7. ☐☐	☐	☐	☐
45-49	8. ☐☐	☐	☐	☐

P.T.O.

If you have now had, or in the past have had, a continuous period of involuntary infertility of <u>at least two years duration</u>, please answer the following questions:-

(13) Please give total duration of period(s) of involuntary infertility.

..... years

☐☐ 50-51

(14) Were you in anaesthetic practice during the period(s) of involuntary infertility?

(a) Whole time Yes/No ☐ 52

(b) Part time Yes/No ☐ 53

(15) Has a cause of the infertility been determined in your or your husband? Yes/No ☐ 54

(16) Has a period of involuntary infertility ever been followed by pregnancy? Yes/No ☐ 55

(17) If yes, were you in anaesthetic employment during the first trimester of such a pregnancy? Yes/No ☐ 56

☐2 80

Please enter any additional comments which you think would help the survey:

UNIVERSITY OF GLASGOW

CONFIDENTIAL ENQUIRY INTO THE POSSIBLE EFFECTS

OF ANAESTHETIC PRACTICE ON PREGNANCY

SURVEY OF WOMEN MEDICAL GRADUATES

It is most important that you should return this questionnaire. The results will be inconclusive unless a high return rate is obtained.

Your name and address will be seen only by one of three doctors and all questionnaires will be destroyed at the conclusion of the survey. Any publications which result from this survey will not permit the identification of any individual.

If you are unmarried, and have never been married, then you need answer questions 1 to 5 only, but please return the form.

If you are married, or have been married, please answer all the questions.

Please pay special attention to the wording of questions 7 and 11.

Please do not write anything within the boxes.

****

(1) Name (capital letters)

(2) Address (capital letters) ☐☐☐☐☐ 1-5

---

(3) Are you, or have you been in anaesthetic practice? Yes/No ☐ 6

(4) Have you completed our similar questionnaire designed for anaesthetists? Yes/No ☐ 7

(5) Are you, or have you been married? Yes/No ☐ 8

(6) Age ..... years ☐☐ 9-10

P.T.O.

(7) Please complete the following table for all pregnancies of AT LEAST 28 WEEKS DURATION. Enter them in chronological order. Twins should appear as two separate consecutive entries. Other multiple births should be entered likewise. If there are more than eight children, enter the first eight only.

	Maturity at delivery (weeks)	Was the child born alive? (yes/no)	If born alive did the child die within 4 weeks? (yes/no)	Sex of child	Congenital abnormalities (please specify)	
1.	☐☐	☐	☐	☐	☐	17-22
2.	☐☐	☐	☐	☐	☐	25-30
3.	☐☐	☐	☐	☐	☐	33-38
4.	☐☐	☐	☐	☐	☐	41-46
5.	☐☐	☐	☐	☐	☐	49-54
6.	☐☐	☐	☐	☐	☐	57-62
7.	☐☐	☐	☐	☐	☐	65-70
8.	☐☐	☐	☐	☐	☐	73-78

(8) Have you had more than eight children? Yes/No ☐ 6

(9) How many twin pregnancies have been entered? ..... ☐ 7

(10) How many multiple pregnancies other than twins have been entered? ..... ☐ 8

(11) Please complete the following table for all pregnancies which terminated spontaneously BEFORE THE 28TH WEEK OF GESTATION:-

	Maturity (weeks)			Other information (e.g. congenital abnormality or known cause for miscarriage)
10 - 14	1. ☐☐	☐	☐	☐
15 - 19	2. ☐☐	☐	☐	☐
20 - 24	3. ☐☐	☐	☐	☐
25 - 29	4. ☐☐	☐	☐	☐
30 - 34	5. ☐☐	☐	☐	☐
35 - 39	6. ☐☐	☐	☐	☐
40 - 44	7. ☐☐	☐	☐	☐
45 - 49	8. ☐☐	☐	☐	☐

P. T. O.

If you have now had, or in the past have had, a continuous period of involuntary infertility of at least two years duration, please answer the following questions:-

(12) Please give duration of period(s) of involuntary infertility ..... years [ ][ ] 50-51

(13) Has a cause of the infertility been determined in yourself or your husband? Yes/No [ ] 54

(14) Has a period of involuntary infertility ever been followed by pregnancy? Yes/No [ ] 55

[2] 80

Please enter any additional comments which you think would help the survey:

APPENDIX C

UNIVERSITY OF GLASGOW

ALASTAIR A. SPENCE
M.B., Ch.B., F.F.A.R.C.S.
Senior Lecturer

4, LILYBANK GARDENS,
GLASGOW, W.2.
TEL: 041-339-8855, Ext. 7150

DEPARTMENT OF ANAESTHESIA (WESTERN INFIRMARY)

May, 1971.

LETTER TO LADY ANAESTHETISTS

Dear Doctor,

A recent survey has suggested that there may be an abnormally high rate of spontaneous abortions among women anaesthetists in Scandinavia.

In collaboration with the University Departments of Statistics and Medicine in Relation to Mathematics and Computing, we are conducting a survey among women anaesthetists in the United Kingdom to assess, as accurately as possible, the incidence of spontaneous abortion, foetal abnormality and involuntary infertility in women who are, or have been, in anaesthetic practice.

We are sending this questionnaire to lady members of the various local and national anaesthetic societies and associations and also to Fellows in the Faculty of Anaesthetists. Therefore, it could happen that you may receiv this questionnaire more than once. In that case, would you please return any extra copy and write the word "duplicate" on it.

This important information cannot be obtained without asking personal questions and we hope that you will not regard this questionnaire as too great an intrusion upon your privacy. We have given much thought to the use of an anonymous reply system. However, the need to follow up questionnaires which may not be returned compels us to employ a system which would enable you to be identified from the reply form. We assure you that these replies will be treated with strict confidence. All questionnaires will be destroyed on completion of the survey.

You will appreciate that we have no information on the maritial status of the anaesthetists on our lists. Should the questionnaire be inapplicable, we ask only that you answer questions one to six and return the questionnaire. A survey of this type is totally dependent on a very high response rate and we respectfully urge you to return this questionnaire promptly.

Yours sincerely,

Donald D. Moir

Lucia V. Rodrigues

Alastair A. Spe

Donald D. Moir,
Consultant Anaesthetist.

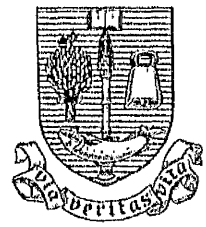
Lucia V. Rodrigues,
Registrar in Anaesthetics.

Alastair A. Spen
Senior Lecturer a
Honorary Con. Ana

APPENDIX D

UNIVERSITY OF GLASGOW

ALASTAIR A. SPENCE
M.B., Ch.B., F.F.A.R.C.S.
Senior Lecturer



4, LILYBANK GARDENS,
GLASGOW, W.2.
TEL: 041-339-8855, EXT. 7150

DEPARTMENT OF ANAESTHESIA (WESTERN INFIRMARY)

May, 1971.

LETTER TO WOMEN MEDICAL GRADUATES

Dear Doctor,

A recent survey has suggested that there may be an abnormally high rate of spontaneous abortions among women practicing anaesthesia in Scandinavia. You may be aware that many appointments in anaesthesia in this country are held by women and you will appreciate the importance of determining whether or not the Scandinavian findings are relevant to the United Kingdom.

A detailed questionnaire has been sent to all women known to be in anaesthetic practice enquiring about spontaneous abortion, foetal abnormality and involuntary infertility. However, there are no reliable figures from the rest of the community to allow comparison and we are asking randomly selected lady doctors on the General Medical Register to answer the enclosed modified questionnaire. We hope you will be willing to help us.

This important information cannot be obtained without asking personal questions and we hope that you will not regard this questionnaire as too great an intrusion upon your privacy. We have given much thought to the use of an anonymous reply system. However, the need to follow up questionnaires which may not be returned compels us to employ a system which would enable you to be identified from the reply form. We assure you that these replies will be treated with strict confidence. All questionnaires will be destroyed on completion of the survey.

You will appreciate that there is little information in the Register on the maritial status of doctors. Should this questionnaire be inapplicable, we ask you to answer questions 1 to 6 only and return the form.

There is an unavoidable 1 in 15 chance that this questionnaire will be sent to a lady in anaesthetic practice and who will also have received the form designed for anaesthetists. In that event, would you please answer questions 1 to 4 only.

Finally, a survey of this type is totally dependent on a very high respons rate and we respectfully urge you to return this questionnaire promptly.

Yours sincerely,

Donald D. Moir

Donald D. Moir,
Consultant Anaesthetist.

Lucia V. Rodrigues

Lucia V. Rodrigues,
Registrar in Anaesthetics.

Alastair A. Spence

Alastair A. Spence,
Senior Lecturer and
Honorary Con. Anaes.

APPENDIX E

UNIVERSITY OF GLASGOW

ALASTAIR A. SPENCE
M.B., Ch.B., F.F.A.R.C.S.
Senior Lecturer

4, LILYBANK GARDENS,
GLASGOW, W.2.
TEL: 041-339-8855, Ext. 7150

DEPARTMENT OF ANAESTHESIA (WESTERN INFIRMARY)

AAS:mw

August, 1971.

Dear Doctor,

Some weeks ago, we wrote to ask for your help with a survey which this department is conducting. Since we have no record of receiving a reply from you and in case you did not receive the original document, I am enclosing a duplicate questionnaire and explanatory letter in the hope that you will help us before our proposed closing date of 30th September. So far, we have a reply rate of 70% which means that, with your help, it is likely that we will be able to provide a meaningful answer to the important and anxious questions which are the reason for the survey.

A few ladies have asked that they be allowed to reply anonymously. We have given our reasons for not employing this system. However, an accurately completed anonymous reply is preferable to no reply, and we would value such co-operation. Some doctors have written to suggest that, since they are not married, the survey is not relevant and we emphasise that we would like them to answer the initial questions and return the questionnaire.

Finally, we apologise to doctors who have already returned duplicate questionnaires and who are being troubled again. We regret that, because our previous instructions were not clear, we have received a number of forms marked "duplicate" but have no means of knowing who has sent them. We hope that these long suffering ladies will be willing to write "duplicate" on the enclosed form together with their name and address.

Yours sincerely

Alastair A. Spence

Alastair A. Spence

APPENDIX G

UNIVERSITY OF GLASGOW

ALASTAIR A. SPENCE
M.B., Ch.B., F.F.A.R.C.S.
Senior Lecturer

4, LILYBANK GARDENS,
GLASGOW G12 8RZ

TEL: 041-339 8855, Ext. 7150
and
041-339 8822, Ext. 159

DEPARTMENT OF ANAESTHESIA (WESTERN INFIRMARY)

Your Ref:
Our Ref: AAS:mw

May 1973

ANAESTHETIC PRACTICE AND OBSTETRIC HISTORY

Letter to Anaesthetists and Other Doctors in the United Kingdom

Dear Doctor:

You may be aware, from reports in the medical press*, that there is considerable anxiety about the possibility of obstetric mishap associated with employment in anaesthesia and perhaps other occupations associated with operating theatres. Apart from the problem of personal distress, these reports may have important implications for the choice of drugs used in anaesthesia and also for the design of operating theatres. It is now very important to find out whether the wives of male anaesthetists and others who work in operating theatres have an abnormal pattern of obstetric history. It is not possible to assess this without a comparable control group. For this reason, we are writing to all male anaesthetists in the United Kingdom and a selected number of doctors in other branches of medicine asking them if they will agree to supply information on the obstetric history of their marriage and also about other specific health problems.

I hope very much that you will agree to help us in this matter. The enclosed questionary appears at first to be formidable but in fact it should take not more than five to ten minutes of your time. This survey in the U.K. is being conducted in parallel with a similar enquiry in the United States.

The nature of the investigation requires that we ask a number of personal questions and we hope you will not regard this as an undue intrusion on your privacy. All replies will be treated with the strictest confidence. No names are, or will be, attached to the reply forms although the number on the form is an identification which will be used only to check the replies and for follow-up should any reply be difficult to interpret. Those members of this University who will be responsible for processing the data will not be able to identify the respondent.

Because of the difficulties in compiling a list of anaesthetists, it may be that a few doctors will receive more than one form. In that event, we would be grateful if you would complete only one form in the manner requested and return the other, without completing it, marked "duplicate" together with your name and address.

I do hope we can count on your help and thank you in anticipation of an early reply.

Yours sincerely

Alastair A. Spence

Alastair A. Spence

* for example: Lancet (1972) 2, 519.

APPENDIX H

UNIVERSITY OF GLASGOW

ALASTAIR A. SPENCE
M.B., Ch.B., F.F.A.R.C.S.
Senior Lecturer

4, LILYBANK GARDENS,
GLASGOW G12 8RZ

TEL: 041-339 8855, Ext. 7150
and
041-339 8822, Ext. 159

DEPARTMENT OF ANAESTHESIA (WESTERN INFIRMARY)

Your Ref:
Our Ref: AAS:mw

September 1973

LETTER TO MALE MEDICAL PRACTITIONERS IN THE U.K.

Dear Doctor:

In the early part of the summer, I wrote to you in connection with a survey which we are conducting on the obstetric histories of the wives of male medical practitioners. A copy of the letter is printed in a reduced form overleaf. This study is designed to determine whether there is a special health hazard associated with working in an operating theatre. However, it is important to obtain information about all types of medical practitioners so that acceptable comparisons can be made. The information which we seek and the conclusions which can be drawn from the enquiry is of great importance to many members of the medical profession.

Since we have no record of a reply from you, I write to ask whether you would agree to reply on the enclosed form. Although we have had a good response to date, it is important that we obtain the highest possible reply rate before commencing analysis of the figures. Your co-operation would be greatly appreciated and I do hope you will agree to help.

If because of any administrative fault on our part you have replied in this survey already, would you please return the enclosed form in the envelope provided. The form should be marked "duplicate".

Yours sincerely

Alastair A. Spence

Alastair A. Spence

EFFECTS OF WASTE ANESTHETICS ON HEALTH

APPENDIX I

File Number - [0] (1-7)

Form Approved
OMB No. 68-R1331

INSTRUCTIONS: This form should take only 5 to 10 minutes to fill out. Print numbers clearly in the appropriate boxes. Most answers require only a check. Please fill out both sides of the page.

Soc. Sec. No. [ ][ ][ ][ ][ ][ ][ ][ ][ ] (8-16) Birthdate: Mo. [ ][ ] Year 19[ ][ ] (17-20) Sex: M [ ] F [ ] (21)

WORKING ENVIRONMENT: Check area of your primary assignment (only one check for each year)

Year	OR	ICU	OB	Dental	Other hospital duties	Not working in hospital	
1963							(22)
1964							(23)
1965							(24)
1966							(25)
1967							(26)
1968							(27)
1969							(28)
1970							(29)
1971							(30)
1972							(31)

If you have not worked in the OR during the past 5 years, disregard the next four questions:

Are your operating rooms air-conditioned? ..... Yes [ ] No [ ] Don't Know [ ] (32)

Is this a recirculating ventilating system? ..... Yes [ ] No [ ] Don't Know [ ] (33)

Are overflow anesthetic gases currently exhausted from the OR? ..... Yes [ ] No [ ] Don't Know [ ] (34)

If yes, when was this system completed? ..... Month [ ][ ] Year 19[ ][ ] (35-38) Don't Know [ ] (39)

QUESTIONS CONCERNING YOUR OWN HEALTH:

Have you ever had cancer or leukemia? ..... Yes [ ] No [ ] (40)

If yes, year of onset ..... 19[ ][ ] (41-42)

Diagnosis: site _____ type _____

Have you had other health problems during the past 10 years?

Liver? ..... Yes [ ] No [ ] (43) Diagnosis _____

Kidney? ..... Yes [ ] No [ ] (44) Diagnosis _____

Other? ..... Yes [ ] No [ ] (45) Diagnosis _____

QUESTIONS CONCERNING YOUR PREGNANCY HISTORY:

(For males, this section applies to your wife)

Have you been studied for infertility? ..... Yes [ ] No [ ] (46)

If yes, what was the diagnosis? _____

Was an abnormality found? ..... Yes [ ] No [ ] (47)

Total number of pregnancies ..... [ ][ ] (48-49)
(Include all pregnancies and miscarriages)

Additional comments after completing questionnaire: _____

NIOSH – 18 (CIN)
1/73

★U.S. GOVERNMENT PRINTING OFFICE: 1972--756-168

PREGNANCY HISTORY DURING PAST 10 YEARS: (For males, the following questions pertain to your spouse(s)). Use a separate line for each pregnancy (including miscarriages). In the event of multiple births, list each child individually.

No.	Age of Mother	Date of Birth or Abortion		Week of gestation	RESULT OF PREGNANCY						TRIMESTER Check if either parent was working in the O.R. during pregnancy.						CONTRACEPTION within 12 months prior to pregnancy		
					Weight		Sex		Stillborn		Abortion		1st		2nd		3rd				
		Month	Year		lbs.	oz.	M	F	Yes	No	Spont.	Therap.	Mother	Father	Mother	Father	Mother	Father	None	Pill	Other
(7)	(8-9)	(10-11)	(12-13)	(14-15)	(16-17)	(18-19)	(20)	(21)	(22)	(23)	(24)	(25)	(26)	(27)	(28)	(29)	(30)	(31)	(32)	(33)	(34)
1			19																		
2			19																		
3			19																		
4			19																		
5			19																		
6			19																		
7			19																		
8			19																		

No.	PREGNANCY HISTORY						HEALTH OF CHILDREN BORN DURING PAST 10 YEARS									
	Smoking during pregnancy (cigarettes/day)			Rubella during pregnancy		Abdominal X-ray or pelvimetry	Congenital Abnormalities (See Table* & list each by letter & number from left. e.g.-anencephaly = E 1 .)			Cancer or Leukemia					Death of Child		
												Age at	Diagnosis				
	None	Under 20	Over 20	Yes	No	Yes No				Yes	No	Onset	Site	Type	Yes	No	Cause
	(35)	(36)	(37)	(38)	(39)	(40) (41)	(42-43)	(44-45)	(46-47)	(48)	(49)	(50-51)			(52)	(53)	
1																	
2																	
3																	
4																	
5																	
6																	
7																	
8																	

*Table of Congenital Abnormalities:
A. cardiovascular: 1. atrial septal defect 2. ventricular septal defect 3. patent ductus 4. other
B. respiratory: 1. choanal atresia 2. diaphragmatic hernia 3. agenesis of lung 4. other
C. musculoskeletal: 1. achondrodysplasia 2. syndactyly 3. limb amputation 4. other
D. gastro-intestinal: 1. cleft palate or lip 2. imperforate anus 3. omphalocoele 4. other
E. central nervous system: 1. anencephaly 2. spina bifida 3. hydrocephalus 4. other
F. urogenital: 1. extrophy of bladder 2. hypospadias 3. undescended testicle 4. other
G. skin: 1. cavernous hemangioma 2. birthmark 3. nevus 4. other

SECTION 3 – WORKING ENVIRONMENT:

Please tick your primary occupation for each year.

Last Card Col. 15 Zero		Anaesthesia	Surgery	Radiology	Other Hospital Work	Not in Hospital
	Code:-	1	2	3	4	5
1963	16	☐	☐	☐	☐	☐
1964	17	☐	☐	☐	☐	☐
1965	18	☐	☐	☐	☐	☐
1966	19	☐	☐	☐	☐	☐
1967	20	☐	☐	☐	☐	☐
1968	21	☐	☐	☐	☐	☐
1969	22	☐	☐	☐	☐	☐
1970	23	☐	☐	☐	☐	☐
1971	24	☐	☐	☐	☐	☐
1972	25	☐	☐	☐	☐	☐
	Code:-	1	2	3	4	5

SECTION 4 – QUESTIONS CONCERNING YOUR OWN HEALTH:

Col.

26 Have you ever had cancer or leukemia? *Yes* ☐

No ☐

27-28 If yes, year of onset 19☐☐

Diagnosis – site ..... type .....

Have you had major health problems during the past ten years?

29 Liver? – *Yes* ☐ *No* ☐ Diagnosis .....

30 Kidney? – *Yes* ☐ *No* ☐ Diagnosis .....

31 Other – *Yes* ☐ *No* ☐ Diagnosis .....

Please enter any comments:

APPENDIX F

№ 20891

UNIVERSITY OF GLASGOW

CONFIDENTIAL ENQUIRY INTO THE POSSIBLE EFFECTS OF ANAESTHETIC PRACTICE ON PREGNANCY

We respectfully urge you to return this questionary. Without a high return, results are conclusive.

If you are unmarried, please ignore Sections 1 and 2.

If you are married, please answer all questions carefully.

If you have been married more than once, please enter the obstetric history as if for c marriage.

Most questions require only a tick in the appropriate box. A few require numbers, e.g. year of birth 1947: enter as 19 | 4 | 7 |.

Are you or have you been married? *Yes* ☐ *No* ☐ Co (

Year of your birth 19☐☐ 7-

SECTION 1 – INFERTILITY:

Have you had a period of *involuntary* infertility of more than 2 years duration? *Yes* ☐ *No* ☐ (

If so, has a cause been determined in you or your wife? *Yes* ☐ *No* ☐ 1(

Were you working regularly in an operating theatre during the period(s) of infertility? *Yes* ☐ *No* ☐ 1

SECTION 2 – PREGNANCY HISTORY:

These questions relate to your wife(s). Use a separate line for each pregnancy *including miscarriages, and enter the events in chronological order.*

For multiple births, enter each child individually. Where there are more than nine pregnancies, enter the first nine only.

	MOTHER'S HEALTH DURING PREGNANCY						TICK IF PARENTS WORKING IN AN OPERATING THEATRE						BABY					SPONTANEOUS ABORTION (Maturity 28 weeks or less)					HEALTH OF CHILDREN						
Col. 15	16-17	18		19		20	21	22	23	24	25	26	27-28	29-30	31-32	33	34	35	36		37-38	39-40	41-42	43		44-45	46-47	48		49-50
	Age	*Smoking*		*Rubella*		*Abdominal X-Ray*	*1st Trimester*		*2nd Trimester*		*3rd Trimester*		*Weight*		*Maturity*	*Sex*		*Stillborn*			*Week of*	*Known Cause*	*Please specify*			*Cancer or Leukaemia*			*Death of Child*	
Card No.		*Yes*	*No*	*Yes*	*No*	*Yes*	*Mother*	*Father*	*Mother*	*Father*	*Mother*	*Father*	*lb.*	*oz.*	*Weeks*	*M*	*F*	*Yes*	*No*	*Yes*	*Gestation*	*(Please Specify)*	*any Congenital Abnormalities*	*Yes*	*No*	*Age of Onset*	*Site - Type*	*Yes*	*No*	*Cause*
1.																														1.
2.																														2.
3.																														3.
4.																														4.
5.																														5.
6.																														6.
7.																														7.
8.																														8.
9.																														9.

[P.T.O.