IS THERE A HEALTH HAZARD IN ANAESTHETIC PRACTICE?

A. A. SPENCE AND R. P. KNILL-JONES

Although it is a fact that the operating theatre environment is contaminated by anaesthetic gases which are taken up by the body tissues of theatre personnel, and although for the past 10 years and more there have been investigations of the consequences for health, there is still no direct evidence that this contamination is a health hazard. However, there is much indirect and circumstantial evidence, reviewed here, which, in the opinion of most observers, justifies fully both concern about contamination of theatre air and measures to reduce it.

METHODS OF STUDY

There are four ways in which the toxicity of theatre pollution can be investigated. All have major limitations and disadvantages.

Animal experimentation

While some importance must be attached to studies of the toxicity of inhalation anaesthetic agents in doses sufficient to cause surgical anaesthesia, there is a need for an experimental model which will simulate the theatre worker in a contaminated environment. The first difficulty is to know the appropriate time-dose profile. For example, superficially it might seem satisfactory to expose an animal to halothane and nitrous oxide in the likely average concentrations for an unsavaged operating theatre. However, actual human exposure is different; the anaesthetist may move frequently from the recovery room, where the amounts of contamination are likely to be small (Pfaffli, Nikki and Ahlman, 1972), to within a short distance of an expiratory valve where the concentration may be close to that which is maintaining the patient asleep.

Most studies have been restricted to small animals such as the rat, mouse and rabbit. The need for this on the grounds of handling and cost is obvious, but there remains uncertainty about the relevance of the findings to man; this is particularly true of the studies of teratogenicity and carcinogenicity, both of which are central to the anxieties about theatre pollution.

Experimentation on human volunteers

Obviously, this has a limited application, but valuable information about effects on the immune responses and the patterns of drug metabolism has been obtained.

Epidemiological survey

This has been employed widely. The usual technique is that of a postal survey of anaesthetists or other theatre workers ("exposed") and a comparable group which does not work in an environment contaminated by anaesthetics ("unexposed"). However, reply rates have been less than ideal, varying from 40% to 82% and, in the largest enquiry (Cohen et al., 1974), there was a much greater response from the exposed compared with the unexposed group. Moreover, the numbers available for study are likely to be too small unless the total population (of anaesthetists in the U.K. for example) is surveyed.

It is virtually impossible to conduct such enquiries without explaining the reasons. Thus, a questionnaire headed "Anaesthetic Practice and Pregnancy" may not elicit the same reaction in the anaesthetist and the haemotologist: an individual's memory for illness may vary. For these reasons, the possibility of bias in reporting cannot be excluded. Since interest has focused on spontaneous abortion and foetal malformation, it should be remembered that their frequency in any enquiry is likely to be influenced by the nature and intensity of the questioning.

The value of a retrospective survey of people at work as a method of determining the incidence of potentially fatal diseases such as cancer is clearly limited.

Finally, it cannot be assumed that those who work in an operating theatre are each exposed to anaesthetic agents to the same extent. Although some enquiries have tried to measure the extent of exposure, the result is, at best, an approximation since the anaesthetist has no means of responding accurately.

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Mortality surveys
Retrospective enquiries (Bruce et al., 1968, 1974) have been difficult to interpret because of a small number of reports and anxieties about the appropriateness of the control group. The recent report by Doll and Peto (1977) is of greater value but, as a prospective enquiry, it took more than 20 years to compile.

METABOLISM OF ANAESTHETICS
If the presence of anaesthetic molecules in the tissues does cause a health risk, there are, broadly, four possible mechanisms:
1. Direct effect
2. Mediated effect on the immune response
3. Direct effect of metabolites
4. Mediated effect of metabolites

There have been many demonstrations of the metabolic breakdown of the inhalation anaesthetics by liver enzymes (Van Dyke and Chenoweth, 1965; Kelly and Brown, 1974; Mazze and Cousins, 1974; Rehder and Sessler, 1974; Van Poznak, 1974). Van Dyke (1966) has shown that chronic exposure to low concentrations of at least one anaesthetic, methoxyflurane, is capable of inducing microsomal enzymes in rats and a similar process has been suggested in man (Cascorbi, Blake and Helrich, 1970, 1972). Wood, O'Mally and Stevenson (1974) found that operating theatre staff metabolized antipyrine more rapidly than did a non-exposed control group. The significance of these findings in isolation is difficult to interpret without more information about the toxic effects of the metabolites. Such abnormal metabolic patterns in theatre workers may be simply a harmless natural response to chronic exposure to the anaesthetic agents.

Several authors have suggested that inhalation anaesthetic agents are capable of altering the immune response in animals (Moudgil, 1973) and man (Loftström and Schildt, 1974), but attempts to demonstrate abnormalities in the immune response of anaesthetists, which might be attributed to chronic toxicity, have produced negative results (Salo and Vapaavuori, 1976).

REPRODUCTION AND THE FOETUS
Animal studies
An increased death rate, decreased growth and defects of the neural tube in chick embryos was shown by Smith, Gaub and Moya to be a response to anaesthetic concentrations of halothane (1965a) and nitrous oxide (1965b). These findings were confirmed by Andersen (1968) and Snegireff, Cox and Eastwood (1968).

In experiments in which small animals received anaesthetic doses of inhalation agents, teratogenic effects have been shown for nitrous oxide in the rat (Fink, Shepard and Blandau, 1967; Shepard and Fink, 1968) and the hamster (Bussard et al., 1974), and for halothane in the rat (Basford and Fink, 1968; Doenicke and Wittmann, 1975), mouse (Smith, Usubiaga and Lehrer, 1971) and hamster (Bussard et al., 1974). These various investigators found a variety of developmental abnormalities of the neural groove, such as defects or absence of ribs and vertebrae. However, two recent detailed studies failed to show any teratogenic effects of halothane in the rat and rabbit (Kennedy et al., 1976; Lansdown et al., 1976).

Shepard and Fink (1968) described resorption of the rat foetus (a process analogous to spontaneous abortion in humans) in association with prolonged nitrous oxide anaesthesia. Bussard and others (1974) confirmed these observations and showed a similar effect for halothane. Doenicke and others (1975) found resorption following halothane but not nitrous oxide.

A crucial experiment would be to demonstrate that prolonged exposure of these species to trace concentrations (such as may contaminate an operating theatre) also caused foetal abnormality, death or resorption. Such studies are very complex to perform. Corbett and others (1973) found that exposure to trace concentrations of nitrous oxide caused an increased foetal death rate and a reduced average number of offspring, but Bruce (1973) and Lansdown and others (1976), studying the effects of trace concentrations of halothane on the pregnant mouse and rat, found no evidence of disturbed foetal development.

Epidemiological studies
Three early studies in the U.S.S.R. (Vaisman, 1967), Denmark (Askrog and Harvald, 1970) and California (Cohen, Bellville and Brown, 1971) all concluded that prima facie there might be an association between anaesthetic practice by pregnant women and an increased frequency of spontaneous abortion. The Danish survey suggested also that there was an effect on the abortion rate of the wives of male anaesthetists, although these women had not been exposed to the theatre environment themselves. Both the Danish and Californian studies found an increased frequency of congenital abnormality of liveborn children associated with anaesthetic practice. Because of the small numbers surveyed or limitations of design, or both, these three investigations could not be regarded as more than pilot studies.
Three large surveys, two in the U.K. (Knill-Jones et al., 1972; Knill-Jones, Newman and Spence, 1975) and one in the U.S.A. (Cohen et al., 1974) yielded retrospective data on the obstetric history of female anaesthetists and the spouses of male anaesthetists, with control groups. The U.S.A. enquiry was extended to include nurse anaesthetists and operating room nurses. A comparative analysis (table I) of the data from these three surveys (Spence et al., 1978) showed remarkable agreement between the two countries in respect of an increased risk of abortion associated with anaesthetic practice by the female, but not the male, although both male and female anaesthetists reported an increase in foetal abnormality in their children in both countries. In addition, female anaesthetists in the U.K. (Knill-Jones et al., 1972) reported involuntary infertility twice as often (12%) as the control group (6%).

In a study of U.S.A. dentists (Cohen et al., 1975), the wives of exposed males had a frequency of spontaneous abortion (16%) significantly greater than had wives of unexposed males (9%), although there was no difference between the groups in the reporting of congenital abnormality.

Rosenberg and Kirves (1973) found that nurses who worked in anaesthesia had a frequency of spontaneous abortion greater than those who worked in a casualty department (15% v. 8.3%) but less than that of "scrub" nurses (21.5%) and intensive care nurses (16.7%).

Pharaoh and others (1977) also surveyed the obstetric history of female doctors in the U.K., but that enquiry failed to yield statistically significant differences in the rates of spontaneous abortion and foetal abnormality between exposed and non-exposed subjects. In the 1975 survey by Knill-Jones, Newman and Spence, however, although this was directed at male doctors, it was possible to identify a small cohort of exposed wives. Their pregnancies were matched with those of control subjects for age, smoking habit and parity—a method of analysis which is more precise than that of calculating group

**Table I. Adjusted rates from combined U.S.A. and U.K. surveys. Taken from Spence and others (1978) with permission of the Editor of the Journal of the American Medical Association**

<table>
<thead>
<tr>
<th></th>
<th>Age (yr)</th>
<th>Preganacies</th>
<th>Miscarriages/ pregnancies (%)</th>
<th>Live-born children</th>
<th>Congenital abnormalities/ live-born children (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposed female anaesthetists</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>41.6</td>
<td>596</td>
<td>15.7 ± 1.5</td>
<td>494</td>
<td>5.5 ± 1.0</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>39.3</td>
<td>737</td>
<td>17.5 ± 1.4</td>
<td>599</td>
<td>5.5 ± 0.9</td>
</tr>
<tr>
<td>Combined data</td>
<td>—</td>
<td>1333</td>
<td>16.7 ± 1.0</td>
<td>1093</td>
<td>5.5 ± 0.7</td>
</tr>
<tr>
<td><strong>Control female physicians</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>47.2</td>
<td>355</td>
<td>9.6 ± 1.6†</td>
<td>313</td>
<td>2.8 ± 0.9</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>41.8</td>
<td>2150</td>
<td>14.0 ± 0.8</td>
<td>1817</td>
<td>4.2 ± 0.4</td>
</tr>
<tr>
<td>Combined data</td>
<td>—</td>
<td>2505</td>
<td>13.3 ± 0.7</td>
<td>2130</td>
<td>4.0 ± 0.4</td>
</tr>
<tr>
<td><strong>Significance for combined data</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$P &lt; 0.001$</td>
<td>$P = 0.04$</td>
</tr>
<tr>
<td><strong>Exposed male anaesthetists</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>45.2</td>
<td></td>
<td></td>
<td>4143</td>
<td>12.1 ± 0.5</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>39.8</td>
<td></td>
<td></td>
<td>1382</td>
<td>13.9 ± 0.9</td>
</tr>
<tr>
<td>Combined data</td>
<td>—</td>
<td>5525</td>
<td>12.6 ± 0.5</td>
<td>4777</td>
<td>5.0 ± 0.3</td>
</tr>
<tr>
<td><strong>Control male physicians</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>51.8</td>
<td></td>
<td></td>
<td>2261</td>
<td>12.0 ± 0.7</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>41.6</td>
<td></td>
<td></td>
<td>2493</td>
<td>11.5 ± 0.6</td>
</tr>
<tr>
<td>Combined data</td>
<td>—</td>
<td>4754</td>
<td>11.7 ± 0.5</td>
<td>4144</td>
<td>3.7 ± 0.3</td>
</tr>
<tr>
<td><strong>Significance for combined data</strong></td>
<td></td>
<td></td>
<td></td>
<td>$P = 0.10$</td>
<td>$P &lt; 0.001$</td>
</tr>
</tbody>
</table>

* Adjusted rates (+ SEM) from combined surveys of female physicians in the United States and United Kingdom. Rates are per 100; skin abnormalities are excluded.
† Adjusted rates (+ SEM) from combined surveys of male physicians' wives in the United States and United Kingdom. Rates are per 100; skin abnormalities are excluded.
‡ Difference between U.S.A. and U.K. control groups is significant ($P = 0.01$).
§ Student's $t$ test for differences ($D$) in proportion where $t = D/SEM (D)$, and SEM/D is root sum of squared SEMs. $P$ values are one-tailed.
|| Fathers' ages.
¶ Surgeons and radiologists excluded.
averages. It was found that the exposed subjects had an increased risk of spontaneous abortion in the range 158–271%.

Thus, with the exception of Pharaoh and others (1977), the results of all the surveys have pointed to an association between anaesthetic practice and spontaneous abortion, although the conclusions about foetal abnormality are perhaps less precise. Taken in conjunction with the U.K. finding of an increase in involuntary infertility in women anaesthetists, it is tempting to propose a triad of foetal mishap which might be attributed to a single cause—drug-induced abnormality of foetal development as a result of occupational exposure to anaesthetic gases.

However, no attempt has been made to repeat the findings of infertility in any other population of anaesthetists. Moreover, the data on congenital abnormality have never yielded a specific pattern of system involvement, such as neural groove defects which are known to be associated with drug toxicity, to explain the increase in reporting. Knill-Jones, Newman and Spence (1975) have suggested that much of the increased frequency associated with operating theatre work could be explained on the basis of an increase in "minor" conditions; thus bias in reporting cannot be excluded. On the other hand, Cohen and others (1974) found that the children of operating theatre workers were more likely to suffer multifactorial abnormalities—a recognized feature of a specific teratogen.

Fink and Cullen (1976), while accepting at least the data on abortion, have argued cogently against bland assumptions about pollution. They point, for example, to the studies of Barlow, McElhatton and Morrison (1974) who showed that 24 h of isolation ("stress") on day 14–15 of a mouse pregnancy is associated with disturbances of the plasma corticosterone concentration and the development of cleft palate in the foetus. There have been frequent attempts to associate abnormalities of human pregnancy with stress in the mother (Gorsuch and Key, 1974). Is stress the real culprit? Fink and Cullen think it may be, but the validation of such a hypothesis would be difficult. Stress, unlike pollution, is not obviously capable of elimination or reduction.

OTHER DISEASES

Animal studies

There have been many studies of chronic exposure of experimental animals, mainly rats and mice, to concentrations of inhalation anaesthetics less than those required to produce surgical anaesthesia. Liver damage has occurred following administration of halothane (Chenoweth et al., 1972; Chang et al., 1975a; Stevens et al., 1975), and methoxyflurane, but not diethyl ether (Chenoweth et al., 1972). Nephrotoxicity (Chang et al., 1975b) and neurotoxicity (Chang et al., 1974) have been shown for halothane.

Carcinogenicity

Studies in rats and mice have demonstrated that at least some of the volatile anaesthetic agents are capable of inducing cancer. In some of the experiments, the methods of exposure were unusual; for example, Eschenbrenner (1945) induced hepatomas by repeated oral administration of chloroform to mice, while the report by Lloyd, Moore and Breslin (1975) of the carcinogenicity of trichloroethylene was the result of a similar method of administration to rats. Corbett (1976) induced pulmonary and hepatic neoplasms in the offspring of mice by repeated exposure of the mother, during the pregnancy, and the offspring, after delivery, to 0.1–0.5% isoflurane. This study caused controversy in respect of its design and conclusions but was influential, nevertheless, in a campaign for closer scrutiny of the toxicity of isoflurane (NIOSH, 1977).

Human studies

Concern about the dangers to health associated with anaesthetic practice has been fashionable for more than 50 years. As early as 1922, the readers of the journal *Anesthesia and Analgesia* were presented with an annotation entitled: "Noted anesthetist dies a martyr to his skill" while later reports (Werthmann, 1949; Vaisman, 1967) listed a variety of symptoms which were attributed to environmental pollution by anaesthetics.

Bruce and others (1968) reported causes of death among male members of the American Society of Anesthesiologists with the statistics of a life assurance company for control purposes. There were no statistically significant differences between these two groups, although tumours of the lymphoid and reticulo-endothelial system and suicide were more common, and lung cancer and coronary artery disease were less common, among the anaesthetists. A parallel 5-year prospective study (Bruce et al., 1974) failed to confirm these impressions.

Doll and Peto (1977) surveyed 20,000 male U.K. doctors over a 20-year period. There were 547 deaths among anaesthetists, with no unusual patterns compared with other doctors except that five had died of
HEALTH HAZARDS OF ANAESTHESIA?

cancer of the pancreas whereas only two such deaths were expected statistically.

Cohen and others (1974) and Knill-Jones, Newman and Spence (1975) collected limited information about diseases which had occurred in the previous 10 years other than those of pregnancy. Specific questions were asked about disease of the liver and kidney and about cancer, although the respondents were invited to list other major illnesses which were not specified. The response for U.K. male doctors, which has not been published in full previously, is shown in tables II and III.

Anaesthetists reported major illness more frequently than did other groups of doctors, although none of the differences between them and the next highest reporting category (table II) is statistically significant.

Table III shows the reported disease rates for all respondents divided into three work categories. There was no significant difference between the groups in respect of cancer, and diseases of the kidney, central nervous system and lung. However, anaesthetists had a significantly greater frequency of liver disease, bone and joint disease (notably of the lumbar spine), diseases of the cardiovascular system (arterial hypertension) and of the alimentary tract (peptic ulcer).

A comparison of the U.S.A. and U.K. data for male doctors (Spence et al., 1978) yielded clear evidence that "hepatitis" was more common in anaesthetists than in other doctors, although more specific information is awaited. None of the other risks apparent in the U.K. survey was reflected in the U.S.A. It should be emphasized that much of this information is open to criticism because it was sought only as an addendum to enquiries about obstetric history, and the quality of questioning was poor. In these circumstances, it is difficult to assess the reporting of hypertension and peptic ulcer since there is ample scope for subjective bias in the use of these terms. Moreover, compared with a typical U.K. sample, the level of reporting of hypertension (Hawthorne, Greaves and Beavers, 1974) and peptic ulcer (Cotton, 1973) among anaesthetists is low.

Cancer in women

A retrospective survey of working populations has obvious limitations for the study of cancer.

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**Table II. U.K. male doctors (%) reporting retrospectively major illness in the period 1964-73. Total number of respondents in each group in brackets**

<table>
<thead>
<tr>
<th>Medical practice</th>
<th>Age (yr)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>57-66</td>
<td>47-56</td>
<td>37-46</td>
<td>&lt;37</td>
</tr>
<tr>
<td>Anaesthetists</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>39.5 (210)</td>
<td>31.0 (371)</td>
<td>15.6 (520)</td>
<td>14.7 (306)</td>
</tr>
<tr>
<td>Surgeons</td>
<td>35.3 (85)</td>
<td>25.5 (98)</td>
<td>11.4 (158)</td>
<td>11.9 (151)</td>
</tr>
<tr>
<td>Radiologists</td>
<td>23.8 (21)</td>
<td>5.0 (20)</td>
<td>8.3 (24)</td>
<td>10.0 (10)</td>
</tr>
<tr>
<td>Other hospital staff</td>
<td>26.6 (113)</td>
<td>15.7 (204)</td>
<td>15.9 (220)</td>
<td>9.9 (374)</td>
</tr>
<tr>
<td>Outside hospital</td>
<td>27.0 (415)</td>
<td>20.4 (747)</td>
<td>12.9 (651)</td>
<td>13.1 (313)</td>
</tr>
<tr>
<td>Mixed category/retired</td>
<td>30.0 (20)</td>
<td>41.7 (12)</td>
<td>21.1 (19)</td>
<td>6.5 (414)</td>
</tr>
</tbody>
</table>

**Table III. Male survey, reported disease rates: all replies (5476 respondents—anaesthetists 1407 (25.7%), other hospital 1478 (27.0%), non-hospital 2591 (47.3%)). Numbers replying (percentage)**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Anaesthetists</th>
<th>Other hospital</th>
<th>Non-hospital</th>
<th>P</th>
<th>( \chi^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>22 (1.56)</td>
<td>25 (1.69)</td>
<td>*44 (1.7)</td>
<td>n.s.</td>
<td>0.1</td>
</tr>
<tr>
<td>Liver</td>
<td>*44 (3.13)</td>
<td>36 (2.44)</td>
<td>49 (1.9)</td>
<td>&lt;0.05</td>
<td>6.1</td>
</tr>
<tr>
<td>Kidney</td>
<td>31 (2.22)</td>
<td>*38 (2.57)</td>
<td>62 (2.39)</td>
<td>n.s.</td>
<td>0.4</td>
</tr>
<tr>
<td>Bone and joint</td>
<td>*42 (2.99)</td>
<td>16 (1.08)</td>
<td>40 (1.54)</td>
<td>&lt;0.001</td>
<td>16.5</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>*71 (5.05)</td>
<td>37 (2.5)</td>
<td>106 (4.09)</td>
<td>&lt;0.01</td>
<td>12.9</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>*68 (4.8)</td>
<td>41 (2.77)</td>
<td>93 (3.59)</td>
<td>&lt;0.02</td>
<td>8.74</td>
</tr>
<tr>
<td>C.n.s.</td>
<td>*24 (1.71)</td>
<td>15 (1.01)</td>
<td>28 (1.08)</td>
<td>n.s.</td>
<td>3.7</td>
</tr>
<tr>
<td>Respiratory</td>
<td>*33 (2.35)</td>
<td>20 (1.35)</td>
<td>41 (1.58)</td>
<td>n.s.</td>
<td>4.7</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>*38 (2.7)</td>
<td>38 (2.6)</td>
<td>48 (1.85)</td>
<td>n.s.</td>
<td>3.8</td>
</tr>
</tbody>
</table>

* Doctor group with highest reporting rate.
Nevertheless, two reports have suggested that there is an increased risk of cancer among female operating theatre personnel. That of Corbett and others (1973) is open to serious criticism in that the data were not standardized (the numbers surveyed were small: 525 nurse anaesthetists), the year of diagnosis ranged from 1935 to 1971, the time interval of occupational exposure to onset of disease varied from 0 to 40 years and the control data were inappropriate, being taken from a general population. The findings of Cohen and others (1974) may be viewed more seriously; their female respondents showed an overall increase in cancer among operating theatre workers although, on analysis by site, the only statistically significant increase (P = 0.05) was for leukaemia and lymphoma.

CONCLUSION

It is reasonable to conclude that the risk of spontaneous abortion is increased in association with anaesthetic practice. The effect on foetal development and infertility is less clear but warrants further enquiry. There is no direct evidence to implicate operating theatre contamination by anaesthetics in these disorders, although it is sensible to assume a possible cause and effect relationship and to take reasonable precautions to reduce contamination (Department of Health, 1976; NIOSH, 1977).

There must be reasonable confidence in the findings of an increased risk of hepatitis in anaesthetists, probably as a result of viral infection (Waterson, 1976). However, there are no firm grounds for believing that operating theatre workers, either male or female, are at risk from any other disease. It would be wise to monitor the frequency of cancer in females, perhaps with special emphasis on leukaemia and lymphoma.

The Ad Hoc Committee of the American Society of Anesthesiologists is committed to a 5-year retrospective enquiry, due in 1979. In the United Kingdom, the authors are responsible for a 5-year prospective survey, under the auspices of the Medical Research Council, of the health of all women doctors under the age of 40 years employed in the National Health Service. Also, there are reasonable grounds for urging employing authorities such as the U.K. Department of Health to record and analyse the causes of death in relation to the type of work undertaken.

ACKNOWLEDGEMENT

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