has been reported by Schwender *et al* in patients having cardiac surgery.¹² After sternotomy under general anaesthesia, and before cardiopulmonary bypass grafting, the patients' auditory evoked potentials were recorded and an audiotape of a short version of *Robinson Crusoe* was played to them. When interviewed postoperatively none of the patients had explicit memories of any intraoperative event. But in an implicit memory test using the code word Friday seven of the 30 patients given the tape associated the word Friday with the story of Robinson Crusoe.

These patients all had large amplitude middle latency auditory evoked potentials that were similar to those seen in lightly anaesthetised subjects. Those with no implicit memory of the story had the low amplitude potentials as seen in more deeply anaesthetised subjects. This study could resolve the disagreement about the likelihood of registering new implicit memories during anaesthesia because it suggests that the anaesthetised brain needs to be in a particular state of arousal to register these memories.

Auditory evoked potentials have now also been used to show the graded effects on the brain of many common general anaesthetics. Changes in auditory evoked potentials correlate with changes in explicit memory at low doses of anaesthesia,^{13 14} and Schwender *et al* suggest that the technique could indicate the point where implicit memory of intraoperative events is ablated.¹²

It remains to be seen whether these results are confirmed in wider studies and whether the auditory evoked potentials

will be a useful routine monitor of cognitive function in anaesthetised patients.

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Controlling occupational exposure to anaesthetic gases

Time to establish an exposure standard

For 25 years epidemiological studies have associated occupational exposure to anaesthetic gases with a range of health effects, including neurological, renal, and hepatic disease; reduction in mental performance and manual dexterity; and increased risk of spontaneous abortion and congenital abnormalities in offspring.¹ Most attention has been focused on studies in the 1970s into the outcome of pregnancy among theatre workers, and these undoubtedly stimulated the Department of Health's guidance recommending improvements in the ventilation of operating theatres and the introduction of scavenging systems.²

These environmental improvements, coupled with methodological criticisms of the early reports, have tended to dispel concern. A major 10 year prospective study of 11 000 women doctors in the United Kingdom, which followed them through 13 500 pregnancies till 1986, was also reassuring (R P Knill-Jones, personal communication, 1992). This study did not confirm the earlier work of the 1970s and showed no relation between hours spent in theatre, medical specialty, and reported miscarriages after confirmed pregnancy. Nor was any increase in congenital malformations observed.

In 1992, however, Rowland *et al* showed a significant risk of reduced fertility in female dental assistants exposed to unscavenged nitrous oxide for five hours or more a week.³ They showed a 59% decrease in the probability of conception for any given menstrual cycle in the exposed assistants compared with unexposed assistants. In doing so they not only highlighted the value of an important reproductive outcome measure but also put assessment of the risk of exposure to anaesthetic gases firmly back on to the health and safety agenda.

A recent alert from the United States government's National Institute of Occupational Safety and Health advocates action to dispel any complacency and cites reports which suggest that health care workers may be at risk even when operating theatres are provided with scavenging equipment.⁴ This confirms similar findings in studies of operating theatres in Britain, in which half the personal samples from anaesthetists exceeded an average concentration of nitrous oxide of 100 ppm during the period monitored.⁵ The alert from the National Institute of Occupational Safety and Health emphasises that simply installing a ventilation system and scavenging equipment is not enough. Such technology must be supported by planned preventive maintenance, regular inspections for leaks and defective equipment, and good anaesthetic technique. This should be supported by a commitment to training so that all concerned understand the preventive measures required.

Atmospheric monitoring by personal and background sampling is also recommended as an essential means of checking the effectiveness of control measures. Yet without an agreed occupational exposure standard this becomes a weak link in the chain. An exposure standard is defined as the concentration of an airborne substance, averaged over a reference period, at which, according to current knowledge, there is no evidence that the substance is likely to be injurious to employees. All of the studies undertaken on anaesthetic gases lack precise exposure data, and in these circumstances the setting of standards can never be an exact science. Despite this there is no shortage of bids in this particular auction.

The National Institute of Occupational Safety and

Health starts the bidding with a recommended exposure limit for nitrous oxide of 25 ppm as a time weighted average during the period for which anaesthetics are given, while the standard of the American conference of governmental industrial hygienists is 50 ppm as an eight hour time weighted average. The current proposal of 100 ppm being considered at present by the British Health and Safety Commission⁶ will, if agreed, be implemented next January. Those wishing to bid higher will argue that the resources required to achieve lower concentrations are not appropriate to the degree of risk.

The lowest bid will, of course, require the highest resources. The proposal from the National Institute of Occupational Health and Safety is particularly courageous in this respect, and many would consider the investment required to achieve that standard to be a major burden relative to the risk, particularly in dentistry, paediatric surgery, and delivery rooms in maternity hospitals, where control is more difficult to achieve. The alert goes further in recommending that when nitrous oxide concentrations exceed 25 ppm workers should ensure that they are supplied with respirators similar to those used in asbestos stripping procedures. At this point the practical difficulties of this proposal in a health care environment escalate beyond belief.

A newly published information sheet on waste anaesthetic gases from the Health and Safety Executive reminds

health services managers that the law requires them to ensure that risks are assessed, control measures are provided, and the effectiveness of that control is monitored.⁷ The establishment of an occupational exposure standard for anaesthetic gases is merited on toxicological grounds. It will also clarify the extent of these management responsibilities and encourage a consistent approach throughout the health service. In agreeing on an appropriate concentration for the first time the Health and Safety Commission should bear in mind that all exposure standards, once set, can be amended downwards in the light of fresh data, but only exceptionally upwards.

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The Cochrane Collaboration

Deserves the support of doctors and governments

The International Cochrane Collaboration is two years old. From small beginnings in September 1992 its membership has grown to over 1000 people. It now has eight collaborating centres around the world and international review groups dealing with 30 clinical areas. Its second international meeting last week in Hamilton, Ontario, attracted over 400 people from 20 countries. But despite these signs of success many who could benefit from the collaboration's work, or contribute to it, remain unaware or unsure of its purpose.

Named after the British epidemiologist Archie Cochrane, the collaboration was set up to evaluate the available evidence from randomised controlled trials. Its underlying assumption is that health care interventions will be more effective if they are based on complete and up to date evidence instead of out of date research, anecdote, and conjecture. Its eventual goals are to create a register of all completed and continuing randomised controlled trials; to combine the results of trials that meet set standards of quality; to produce regularly updated systematic reviews or meta-analyses; and to make these reviews widely available in journals, on CD-ROM, and eventually on line through the internet.

With sophisticated computerised databases such as Medline, finding all randomised controlled trials should be a simple matter. But research by Cochrane collaborators has found that about half the 40 000 randomised trials published since 1985 are not retrievable by expert Medline searches. These findings explain why the collaboration places such importance on searching journals by hand. Researchers and some journal editors are volunteering to hand search journals back to 1948, the year that the *BMJ*

published the landmark randomised controlled trial of streptomycin.¹

Even more taxing than non-indexed trials is the problem of finding trials performed but never published. The collaboration does not know how many trials remain unpublished, but the reasons for failure to publish are becoming clearer. Despite assumptions that journal editors are biased against publishing negative results, studies have shown that it is largely authors who do the censoring by deciding not to submit them.² In addition, we do not know how many trials sponsored by the pharmaceutical and tobacco industries remain unpublished. The marketing advantage in withholding research findings is obvious. But so too are the ethical and opportunity costs in terms of patients, time, and money.

Several groups could help to reduce the proportion of unpublished and unregistered trials. Researchers sponsored by industry could insist that they retain the right to disseminate their results. Codes of practice would strengthen their arm. And ethics committees and journals could make it clear that trials submitted for ethical approval or publication would be considered only if they had been registered. The *BMJ* is considering such a policy. Journals can also help by improving the standard of reporting so that reviewers can quickly assess a study's design. Use of structured abstracts, especially those that specify the method of randomisation, is one important contribution to this.

The collaboration has its critics. Some argue that by taking randomisation as its gold standard it will miss vital data from good non-randomised studies, for which methodologies for systematic review exist. Such data are