

## Awareness under anaesthesia

EDITOR,—I believe that Di Brighthouse and John Norman should have put more emphasis on the treatment of patients who have been aware while under anaesthesia.<sup>1</sup> At the second world congress on anaesthetic awareness, held in Atlanta in May, three speakers presented studies on patients who had been aware while under anaesthesia. My paper looked at the treatment of 32 patients who had been aware. I have shown in this group that an early explanation with counselling by an anaesthetist experienced in helping such patients reduces the risk of post-traumatic stress disorder developing. If such a disorder has developed an explanation with counselling can reduce its severity and duration.

I suggest that every anaesthetic department should have an anaesthetist prepared to help patients who have been aware, particularly if another anaesthetic is necessary, as this provides an additional stressor. Clearly with major stress reactions psychological help is needed, and psychiatrists and psychologists who are prepared to help should be identified. Lastly, an anaesthetist who has a patient who says that he or she was aware may find this stressful and also need help.

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1 Brighthouse D, Norman J. To wake in fright. *BMJ* 1992;304:1327. (23 May.)

EDITOR,—Di Brighthouse and John Norman's editorial on awareness under anaesthesia is the latest in a series reviewing the problem and, like its predecessors, comes to no useful conclusion.<sup>1</sup> Apart from cases due to malfunction of equipment, the problem is due to the deliberate administration of inadequate doses of anaesthetic drugs. This practice is possible only when high doses of neuromuscular blocking agents are used to abolish movement of the patient, which in turn abolishes much of the diagnostic information needed to assess the state of anaesthesia.

Techniques involving inadequate doses of anaesthetic drugs additionally expose patients to the risks of excessive response of the autonomic nervous system to surgery. Brighthouse and Norman make no attempt to justify such techniques other than by saying: "It has become fashionable to reduce the inhaled concentration of gaseous and volatile anaesthetics to minimise their other effects."

There are no objective studies showing that such techniques bring any benefit to the patient whatsoever. Neuromuscular blocking drugs were originally introduced to anaesthesia at a time when general anaesthetic drugs were highly unsatisfactory and specifically to solve the problem of access to the abdomen for major surgery. Since then anaesthetic drugs have become much more effective, with a better profile of action permitting effective anaesthesia and rapid recovery, and the need for neuromuscular blocking drugs has radically diminished. Many of these changes seem to have escaped the notice of anaesthetists in Britain, where this problem is most acute.

In patients undergoing surgery after life threatening trauma, when the dose of anaesthetic drugs is kept to a minimum, there is a straightforward choice between the risk of awareness and

the risk of potentially lethal cardiovascular depression. In the case of anaesthesia for caesarean section, while there are grounds for believing that reducing the doses of anaesthetic drugs may help the fetus, no recent cooperative studies between anaesthetists and paediatricians have shed any light on this issue.

In summary, anaesthetists in Britain persist in using the techniques of profound neuromuscular block with inadequate doses of anaesthetic drugs despite evidence of substantive morbidity and no evidence of benefit.

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EDITOR,—Di Brighthouse and John Norman remind readers that there is no totally reliable monitor of intraoperative awareness.<sup>1</sup> Two aspects, however, deserve comment.

Firstly, the word "awareness" is used to indicate "a period when patients are awake during surgery" or the "conscious postoperative recall for events occurring during surgery." This can be confusing to non-anaesthetists.<sup>2</sup>

Secondly, we disagree with the authors' assessment of the isolated forearm technique. We admit that this technique correlates relatively poorly with clinical signs of light anaesthesia, but this is because clinical signs are unreliable. Likewise, because of the amnesic effects of the anaesthetic, the technique cannot be used to predict who will have recall. If a patient moves a hand in response to an intraoperative command or indicates the presence or absence of pain during surgery by appropriate hand squeezing<sup>3</sup> surely this conveys a clear message, irrespective of any clinical signs, regarding the level of conscious processing at that time.

Intraoperative use of the isolated forearm technique shows the unreliability of clinical signs in predicting intraoperative awareness, the high frequency of such awareness with certain anaesthetic techniques, but the rarity of spontaneous postoperative recall.<sup>4,5</sup> Over many years of personal clinical use there has been little evidence of postoperative recall in patients who did not respond to intraoperative commands. Exceptions have been one case in the early days of the technique,<sup>6</sup> one case of failure of the tourniquet, and one patient who made a conscious decision to ignore the commands "because they kept interrupting my lovely dreams."

Brighthouse and Norman base their assessment of the isolated forearm technique on a preliminary abstract<sup>7</sup> (to our knowledge, no follow up paper of the complete study has ever been published). The methodology and conclusions of that study were severely criticised at the time.<sup>8,9</sup> The results showed that no patient responded to commands before surgery started, and, although no data are presented, there is an implication that once surgery started clinical signs indicated that anaesthesia was adequate but surgery proved impossible because of "purposeful movements of the isolated arm." To deal with this the authors deflated the tourniquet to paralyse the arm. We believe that an arm trying to interfere with surgery is a valid indicator of light anaesthesia irrespective of the clinical signs. As regards the other methods proposed for predicting

anaesthetic awareness, the isolated forearm technique is the "nearest we have to a 'gold standard' against which to evaluate these."<sup>10</sup>

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## Risks associated with assisted conception

EDITOR,—M G R Hull and colleagues state that the objective of their study was "to provide reliable prognostic information for couples seeking assisted conception."<sup>1</sup> There seems little doubt from the pregnancy and live birth rates reported that their centre produces impressive results. Such figures will give great encouragement to both subfertile couples and their doctors. But the authors make the very mistakes for which they criticise others, presenting a selective picture of the outcome. By omitting even to mention the possible hazards they run the risk of leaving their medical colleagues and the public seriously underinformed. I write both as a doctor and as a consumer (with my wife) of in vitro fertilisation, and my experience of assisted conception serves to underline my point.

My previously fit wife underwent her first—apparently routine—cycle of in vitro fertilisation treatment at a reputable joint private and NHS unit in London. She became pregnant with twins. Although not apparent at the time, infection was introduced, presumably at egg collection, and she went on to develop ascites and peritonitis and had to have an emergency laparotomy. Postoperatively, she was nursed in the intensive care unit, where she was found to have multiple pulmonary emboli and later developed a perforation of the bowel followed by faecal peritonitis requiring another laparotomy. After the second operation she developed septic shock and required ventilation and inotropic drugs for 10 days. Her recovery was complicated by a bowel fistula, which healed spontaneously. My wife left hospital, no longer pregnant, after three months, a month of which was spent in intensive care.

I realise that such an experience is extremely rare

in vitro fertilisation, but appreciable side effects are unlikely to be so rare. For instance, ovarian hyperstimulation is a known risk despite published advice that it should be preventable.<sup>2</sup> Adequate information about possible morbidity in assisted conception is not made readily available to potential patients, nor are the hazards apparently sufficiently acknowledged by those who deliver the treatments.

Of course, the increasing success of fertility treatments is to be welcomed, but childless couples, in their desperate longing for babies, are only too ready to overlook the possible drawbacks. Fertility specialists therefore have a duty to present comprehensive information about not only the prospects of success but also the risks of assisted conception.

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EDITOR.—M G R Hull and colleagues' article confirms the positive role of assisted conception.<sup>1</sup> We have several comments.

Firstly, Hull and colleagues are right to question the validity of the legal constraint on the number of eggs and embryos that can be transferred in gamete intrafallopian transfer and in vitro fertilisation. This is especially relevant to women aged 40 or above, who have a low chance of becoming pregnant after assisted conception.<sup>2,3</sup> The incidence of multiple pregnancy in this age group is low even when more than three eggs or embryos are transferred, as confirmed in Hull and colleagues' and other studies.<sup>2</sup> We have long argued for flexibility that allows a variable number of eggs or embryos to be transferred to suit the circumstances of individual couples.

Secondly, Hull and colleagues report a significantly higher pregnancy rate with gamete intrafallopian transfer than with in vitro fertilisation or high intrauterine insemination, which also confirms our experience. The difference in pregnancy rates between gamete intrafallopian transfer and in vitro fertilisation has recently narrowed owing to improvements in in vitro fertilisation and because limiting the number of eggs allowed to be transferred in gamete intrafallopian transfer has a greater effect on reducing the pregnancy rate than limiting the number of embryos transferred in in vitro fertilisation.

Thirdly, the authors' projected cumulative pregnancy rate of 82% after six attempts of in vitro fertilisation or gamete intrafallopian transfer is encouraging, but even better results could have been obtained sooner, and with fewer attempts, if cryopreservation of embryos had been available.

The pregnancy rate after replacement of thawed embryos in our centre in 1991 was 28% per frozen embryo replacement (22 out of 79 cycles). During the same year 275 cycles of gamete intrafallopian transfer and 263 cycles of in vitro fertilisation were performed. The clinical pregnancy rate was 32% after gamete intrafallopian transfer and 24% after in vitro fertilisation (40% and 26% respectively for women under 40). Including frozen embryo replacement results in a projected cumulative pregnancy rate of 60% for gamete intrafallopian transfer and 52% for in vitro fertilisation after a single superovulation egg retrieval cycle (69% and 54% respectively for women under 40).

Cryopreservation of suitable embryos should be an integral part of assisted conception programmes to increase cumulative pregnancy rates and reduce costs and the need for repeated superovulation and egg retrieval.

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## Cancer chemotherapy and fertility

EDITOR.—When quality of life during and after cancer chemotherapy is being considered<sup>1</sup> the loss of gonadal function, with the consequence of infertility, should also be taken into account. Increasing numbers of male and female patients are surviving chemotherapy for cancer in childhood and the reproductive years. Reproductive capability may be a major factor when contemplating their prospective quality of life.

Research is in progress at the Royal London Hospital to determine the precise effects of chemotherapy on fertility. Alkylating agents, for instance, have a substantial deleterious action on the gonads, leading to the possibility that chemotherapeutic substitution may give a better prognosis for fertility without prejudicing the outcome of treatment.

We believe that fertility is an important factor in the quality of life and should be discussed during counselling before and after treatment. It should be taken into account when deciding on the timing of chemotherapy and the protocol. If gonadal damage is deemed inevitable then, when possible, gamete preservation should be offered.

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## Steroid receptors in early breast cancer

EDITOR.—In reviewing recent developments in the management of early breast cancer R D Rubens, discussing risk evaluation, plays down the role of measurement of steroid receptor concentrations.<sup>1</sup> Nevertheless, several reports have shown steroid receptor concentrations to have prognostic value in early, node negative breast cancer treated without adjuvant therapy.<sup>2,4</sup>

We have measured, by enzyme immunoassays, oestrogen receptor and progesterone receptor concentrations in tumours (61%  $\leq$  2 cm) of 130 patients entered into a prospective randomised trial comparing different regimens of radiotherapy in women with clinically node negative early breast cancer ( $\leq$  5 cm diameter) treated by conservative surgery. All patients in this trial received adjuvant tamoxifen, being further randomised to either continuous treatment or treatment for two years only; this is particularly relevant when the prognostic value of hormone receptor status is being considered.

After a median follow up of 18 (range 0-41) months our results show that, with a cut off of 20 fmol/mg, negative status for both steroid receptors, but particularly oestrogen receptors, is significantly associated with early recurrence (table). All the patients who developed recurrence were taking tamoxifen at the time, and the length of follow up for patients who were negative and positive for oestrogen receptors was similar. Of other available risk factors (size and grade of tumour, menopausal status, pS2 protein), only the grade of the tumour ( $\chi^2=6.6$ ,  $p<0.02$ ,  $n=96$ ) and

Number of women who were disease free or had recurrence of breast cancer at follow up according to oestrogen receptor and progesterone receptor status

	Oestrogen receptors		Progesterone receptors	
	Negative	Positive	Negative	Positive
Recurrence (n=19)	14	5	13	6
Disease free (n=111)	22	89	42	69
Total	36	94	55	75
	$\chi^2=20.9$ , $p<0.001$		$\chi^2=5.0$ , $p=0.025$	

the oestrogen regulated pS2 protein concentration (radioimmunoassay, cut off 1 ng/ml;  $\chi^2=5.3$ ,  $p<0.05$ ,  $n=83$ ) were significant. Of the eight deaths related to cancer, six were in women who were negative for both oestrogen receptors and progesterone receptors and all were in women who were negative for at least one steroid receptor.

As Rubens points out when discussing adjuvant therapy, oestrogen receptor concentration has recently been shown to correlate highly significantly with a reduction in annual odds of death with adjuvant tamoxifen.<sup>3</sup> Our early results are consistent with this observation and suggest that markers of a functionally intact oestrogen response pathway (PR and pS2) may also have a role in the evaluation of risk. We believe, therefore, that measurement of steroid receptor concentrations in early breast cancer gives valuable prognostic information, particularly for the increasing number of patients treated with adjuvant tamoxifen.

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## Hyponatraemia in children

EDITOR.—Allen I Areiff and colleagues emphasise the need for greater awareness that serious electrolyte disturbances can occur in apparently healthy children.<sup>1</sup> This has important implications as early treatment can appreciably improve their outcome. We treated a previously healthy 11 year old child who suffered serious neurological complications due to water intoxication during a prolonged swimming session with a mixed age group.

On the evening before his admission he trained as a member of the local lifesaving club; swimming for about three hours. During this time he inadvertently swallowed "a lot of water," being splashed by the adult members of the team. Soon after returning home he started vomiting and became agitated and progressively obtunded. There was no history of exposure to toxins or drugs, nor was there any family history of a seizure disorder.