produced in animals by the removal of ethyl alcohol or by varying the amount of Cremophor EL in the formulation between 5% and 20% (Glen, 1980).

Compared with the therapeutic index calculated in 1980, the emulsion formulation seems to be much safer than the previous Cremophor formulation, whereas in 1984 similar therapeutic indices were calculated for both formulations. Our question is: is this difference caused by the materials, or by the methods used in these studies?

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REFERENCES

Sir,—Thank you for giving us the opportunity to respond to the question raised by Drs Ruys and De Grood.

We agree that there is a difference in the therapeutic ratio obtained with Cremophor preparations of ICI 35868(propofol) in the two pharmacological studies quoted. However, in our judgement, this difference is most likely to be the result of biological variation associated with the acute toxicity component of the Therapeutic Ratio. As anaesthetic activity was not altered by varying the amount of Cremophor in the formulation, we think it is unlikely that the use of a more dilute preparation in the first experiment should have influenced the result.

It has long been known that the numerical value of the "formal" LD50 is subject to wide variation arising from quite minor changes in environmental conditions and the physical status of the test animals (Morrison, Quinton and Reinert, 1968; Zbinden and Flury-Roversi, 1981). It is, therefore, not surprising that tests done at different times give slightly different results.

We believe that the two formulations can be compared only in a study conducted at the same time in the same batch of mice. This was the case in the study reported in 1984, in which the therapeutic ratio of the emulsion formulation was not significantly different from that of the earlier Cremophor formulation.

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MODIFICATION TO THE SERVO 900B CPAP/IMV SYSTEM

Sir,—It was with great interest that I read the recent article by Cox and Niblett (1984). We have also observed in our patients a considerable pressure deviation during inspiration and expiration with the Servo 900B when used in CPAP and IMV with PEEP, as well as an inspiratory time delay that produces an increase of inspiratory effort and discomfort for the patient.

We have been using the IMV system suggested by Cox and Niblett (1984) when using the Servo 900B, but in our clinical practice have identified a number of patients who need a gas flow greater than 20 litre min⁻¹ via the reservoir bag. Nevertheless, increasing the gas flow via the reservoir bag beyond 20 litre min⁻¹ activates the upper limit alarm on the expired minute volume. We have avoided this problem by adding more than one reservoir bag to the inspiratory limb. This modification made it possible to decrease the gas flow via the reservoir bags and maintain the airway pressure at a constant value throughout the respiratory cycle, even at high values of CPAP or PEEP.

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REFERENCES

Sir,—Thank you for asking for our comments about the letter written by Dr de Latorre. Dr de Latorre does not specify what clinical criteria he used to determine when a patient requires a larger reservoir. We assume that it would be used to ensure that the peak inspiratory flow rate of the patient did not significantly collapse the reservoir bag, thus keeping AP to a minimum. In a recent article (Roeseleer, Bahertz and Reynaert, 1984) it was stated (without reference) that the work of breathing is directly proportional to AP x AV/VT (the mean inspiratory flow rate). The authors suggested that a 23-litre reservoir bag was useful in reducing the work of breathing! What probably happens is that, the larger the surface area of stretched elastic reservoir bag just before inspiration, the greater the degree of "inspiratory assistance" rendered to the spontaneous breath.

In our experience the 4-litre or 6-litre bag is large enough both to give some inspiratory assistance and to ensure that the peak inspiratory flow is not compromised. We have on occasions been quite close to the expiratory upper alarm limit of the Servo 900B, which is a flow greater than 30 litre min⁻¹, but found that these flow rates were clinically unnecessary. However, we take the point that a larger reservoir bag would enable one to cut down fresh gas flow.

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