MAC can be used to ". . . shed much light on mechanism of action (of anesthetics)." Our studies of the additive effects of anesthetics [7, 8] suggest that if anesthetics exert their effects through hydrate formation [9, 10] they cannot do so through production of a continuous "ice cover." Furthermore, the lack of correlation of MAC with hydrate dissociation pressure, particularly the deviation of the sulfur hexafluoride data, has thrown the hydrate theory of anesthesia into considerable doubt.[11] Last, the superb correlation of MAC and lipid solubility as defined by the oil/gas partition coefficient should serve to focus attention on a hydrophobic site of anesthetic action.[11]

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To the Editor:—The above letters raise some interesting points. Doctor Eger feels that MAC is associated with a special point on the dose–response curve—a point of "prime practical and theoretical significance." We would be cautious about emphasizing a theoretical uniqueness. We suspect that the alveolar concentration just sufficient to render a patient unconscious was not crucial when the laws of chemistry and physics were formed. Anesthesia is still just one expression of a general "depressant" action of anesthetics on the central nervous system. These agents produce other CNS effects at concentrations both below and above MAC. In fact, Doctor Eger himself, after trying to extract one point from a dose–response curve, proceeds in the next two paragraphs to discuss the regions above and below. He too finds it impractical to discuss MAC out of context.

What does "MAC is a universal characteristic of anesthesia" mean? Take it literally and you get "A minimal alveolar concentration just sufficient to produce anesthesia is a universal characteristic of anesthesia." Isn't it trivial to say that all anesthetics have a MAC?

Doctor Eger states that there are many reasons to look at concentrations below MAC, and we agree. In fact, we'd look above MAC as well. But is this any reason to relabel these points? Many end-points on the dose–response curve have already been defined. The introduction of the terms "MAC" and "MAC awake" amounts to little more than renaming these points with regard to the abscissa rather than to the ordinate. (Don't forget that MAC is a *concentration.* There is a tendency to treat it like a response; for example, see Eger's "MAC is but one point in this continuum (of depression)" and "it (MAC) represents an end-point.") The end-point for MAC is essentially entry into Stage III, Plane 1; the end-point for MAC awake is return to Stage I.

We agree that MAC may be used to define

"elbow room," but would like to emphasize that the idea of margin of safety has been around for quite some time.

We still feel that examination of dose–response curves *per se* will not tell us much about mechanism of action. Despite the "superb correlation," we still haven't much idea of what the phenomenon of anesthesia is all about. We would also be cautious about correlations based on only one point in a series of degrees of CNS depression. As we've already indicated, there is no *a priori* physicochemical justification for selecting unconsciousness in preference to other end-points. If we try to anticipate the nature of our ultimate picture of the action of anesthetics, we expect that these agents will be found to exert some action at the cellular level and that the clinically observable signs will stem from this basic action. In this sense, loss of consciousness would be only one of many reflections of a more elementary action. Hence, we are uneasy about singling out loss of consciousness for special treatment.

Like Doctor Bachman, we feel that anesthesia has the nature of a quantal response; hence, it is most appropriately analyzed by techniques developed for such data. There are various ways to do this; Bachman used a log-probit transformation, others may prefer the logistic function or a direct analysis. In any case, appropriate statistical evaluation provides a mechanism for objective calculation of confidence limits on the estimates obtained. "Goodness of fit" determinations do not seem crucial, but Bachman's use of checks for parallelism deserves comment. The slope of his dose–response curve is simply a reflection of the distribution of sensitivity in the population being examined. Parallel curves just indicate similar degrees of variation. Of more interest is the parallelism to which Eger and we refer. As we have pointed out, this can be examined only if more than one end-point is considered.

We want to emphasize that, with the possible exception of the use of MAC to select among theories of anesthesia, our position is not very different from Eger's. For example, we find his use of the second end-point to test for parallelism well worth while, and his additivity studies elegant as well as informative. The role of MAC as a *biological unit of concentraton* is also worth emphasizing. While one might quibble about which end-point should be used for such a normalization, this should not detract from the fact that measuring concentrations relative to that which just produces anesthesia is still the best yardstick available. For example, suppose *in vitro* metabolic studies were reported for an agent used at MAC 1, then regardless of the agent and regardless of the molar concentration or the partial pressure, you could tell that the concentration was not out of line with those relevant to clinical practice.

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Pediatrics

IPPB One hundred and sixty infants with hyaline membrane disease were treated in an intensive care unit. Intermittent positive-pressure breathing was used in 66 infants who developed hypoxia (Pa_{O_2} less than 50 torr) or respiratory failure despite treatment with buffers and oxygen. Orotracheal intubation and a pressure-cycled flow generator were used. Twenty-two, or 33 per cent, of the infants given IPPB survived. Pulmonary infection and intraventricular hemorrhage were the most serious complications. In certain infants with hyaline membrane disease who develop respiratory failure despite intensive therapy, mechanical ventilation can sustain adequate ventilation until the disease resolves. (*Heese, H. deV., and others: Intermittent Positive Pressure Ventilation in Hyaline Membrane Disease, J. Pediat. 76: 183 (Feb.) 1970.*)