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MAC Values of Mixtures

To the Editor:—Twenty years ago Merkel and Eger introduced the term, MAC, to represent anesthetic potency.[1] Since then, Eger has co-authored reports that nitrous oxide lowers MAC of various volatile agents.[2,3] For example, page 274 of Quasha and Eger[3] contains the following: "Similarly, 70% nitrous oxide decreases halothane MAC by 61%[8] and enflurane MAC by 60%.[67]" Although their reference 67 is to studies with isoflurane, not enflurane, the authors' meaning that N_2O reduces the volatile agent required to prevent reaction to noxious stimulus is clear. It is not, however, evidence that one agent changed MAC of another. The MAC of a mixture is simply the sum of the MACs of its component parts. This is not just a semantic question, because calculations of multiples of MAC may be erroneous if this principle is not understood. A letter was sent to every tenth person on every tenth page of the 1983 ASA Directory of Members, for a total of 65 letters. The following questions were asked:

Assuming that:

0.8% halothane in O_2 = 1.0 MAC
50% N_2O in O_2 = (approximately) 0.5 MAC
0.4% halothane in 50% N_2O = 1.0 MAC

Then, what are the MAC values for the following mixtures?

1) 1.6% halothane in 50% N_2O _____
2) 1.0% halothane in 50% N_2O _____
3) 2.0% halothane in 50% N_2O _____

Of 20 replies, 10 gave correct answers and 10 gave incorrect answers. The incorrect answers were, respectively, 4, 2.5, and 5 MAC. These respondents obviously took the value of 0.4% halothane in N_2O, 1.0 MAC, and divided this into the higher halothane concentrations given in the problems. Nine of these 10 were private practitioners and eight of those nine were board certified. The same proportions were found among the 10 who gave the correct answers of 2.5, 1.75, and 3 MAC, respectively.

Although the number queried was small and the response rate low, it appears that a significant population of practicing anesthesiologists do not understand the proper way to calculate MAC of mixtures of agents. This can be done best by regarding the MAC for each agent to be a constant concentration, rather than variable according to the presence or absence of other anesthetics. The reason 0.4% halothane in 50% N_2O is 1 MAC is that 0.5 MAC of each is being given, not that N_2O has "lowered" the MAC of halothane. If more halothane is given, more MAC units are added at the rate of 1.0 MAC per 0.8%. Nitrous oxide, 50%, will contribute about 0.5 MAC, no matter what concentration of halothane is being added to it.

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Wresting or Resting Ventilation

To the Editor:—Are pharmacologic investigations of breathing control in humans no more than tests of drug effects on the response to added CO_2?

Reports appearing in ANESTHESIOLOGY over the past 2 years describe how lumbar epidural morphine, approximately 0.10–0.15 mg/kg, depresses various indexes of the ventilatory response to rebreathing CO_2 in pain-free volunteers and in patient volunteers who have acute or chronic pain.[1–3] Nowhere in these reports did I find mention of the important ventilatory information anesthesiologists are seeking, which is how epidural morphine affects resting ventilation (total and/or alveolar) and resting P_{CO_2} (end-tidal and/or arterial). The ventilatory data of these reports refer only to ventilation stimulated by added CO_2. Several other reports on this subject also focus on the response to CO_2.[4–7]

The ventilatory response to added carbon dioxide frequently has been taken to be a sensitive index of drug

effect on the metabolic regulation of breathing.[8] In the seven studies quoted above, however, it was taken to be, in effect, the sole index of overall ventilatory control. If the CO_2 response is to be used and interpreted in this way, it may be important to consider uncertainties about the test and about the relationship of the response to fundamental variables of ventilatory control–resting ventilation and P_{CO_2}.

The CO_2 stimulus of conventional CO_2 response tests is not relevant to most physiologic circumstances, and the response may not be the same as the response to more physiologically pertinent types of CO_2 stimuli.[9,10] The magnitude of response varies considerably among and within individuals, and this variation does not correlate with resting minute ventilation or end-tidal P_{CO_2}.[11] Effects of drugs on the sensitivity of response appear not to parallel effects on resting breathing and P_{CO_2} in a consistent way—differing quantitatively (*e.g.*, thiopental, morphine, and individual halogenated hydrocarbons) and sometimes even qualitatively (*e.g.*, ether, nitrous oxide and ketamine).[8,12,13] For these and other reasons, effects on the CO_2 response may not be sufficient in themselves for conclusions about how drugs affect relevant aspects of ventilatory control.

In pharmacologic studies of breathing, data on the response to added CO_2 should be supplementary to values of resting ventilation and end-tidal and/or arterial P_{CO_2}. Careful measurements of resting variables always should be reported, no matter how crude or insensitive they might seem. This is crucial and relevant information we need to know.

Let's wrest, not rest, resting ventilation!

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Further Suggestions on Epidural Spread in Pregnancy

To the Editor:—In their report, "Spread of Epidural Analgesia in Early Pregnancy,"[1] Fagraeus *et al.*, state that the compensated alkalosis secondary to hyperventilation during pregnancy favors an increase in the ionized form of local anesthetic agents as compared with the nonionized form (*i.e.*, free base). This argument is used to explain the increased rostral spread of a given dose of local anesthetic agent used for epidural anesthesia in the pregnant state.

Bonica[2] has pointed out that pregnancy results in an incompletely compensated respiratory alkalosis. This has been defined more specifically by Sjostedt[3] as a rise in *p*H of 0.02 by the tenth week of pregnancy.

For a given dose of local anesthetic, the ratio of ionized to un-ionized form is determined uniquely by the pK_a and *p*H through the Henderson–Hasselbach equation. For lidocaine a change in *p*H from 7.40 to 7.42 will increase the un-ionized form from 26.19 to 27.09% a