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"I would have everie man write what he knowes and no more."—Montaigne

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Editorial

Uses of MAC

MAC was first defined in 1963 by Eger and Merkel,[1] in an animal study comparing two agents. In 1964,[2] this was extended to halothane anaesthesia in human subjects. Finally, in 1965,[3] MAC was described as a measure of anaesthetic potency for a number of agents in man. It is defined as the minimum alveolar concentration of anaesthetic at 1 atmosphere (atm), which produces immobility in 50% of subjects exposed to a noxious stimulus, usually a skin incision. Note that concentration is specified; this means that for precision the atmospheric pressure should be quoted when giving a MAC value. If the pressure departs significantly from 1 atm, then this is essential. The difficulty is avoided by expressing MAC as a partial pressure (MAP).

The alveolar concentration of the agent is assumed to be in equilibrium with that in the brain. For this to be a valid assumption, sufficient time must be allowed for the brain concentration to come into equilibrium with that of the lung alveolus before a MAC determination is made. In the original MAC determinations using halothane, a period of 20 min at constant alveolar anaesthetic concentration was considered necessary. This was generous at the time and the lower solubility of modern agents must greatly shorten this time interval. This is a subject on which further work is required. The availability of reliable anaesthetic gas analysers makes it possible to monitor continuously the brain concentration of the agent and this is one of the advantages of inhalation anaesthesia.

The determination of MAC is, by biological standards, a fairly precise procedure. The results of most of the numerous studies on the subject show standard deviations of 10–20%. This is partly attributable to the accuracy of modern anaesthetic gas analysers and the unequivocal nature of the move/not move endpoint. It is now possible to argue that knowledge of the brain concentration of an agent is a better guide to the presence or absence of the anaesthetic state in the patient than other methods of measuring depth of anaesthesia.

The biological variation of MAC is a subject of clinical importance. If a paralysed patient is being ventilated with *x*% of agent *y*, how certain can we be that he is unconscious? The variability of MAC is considered by Sonner.[4]

Anaesthetists have always known that anaesthetic requirements decreased with age. Guedel in 1937,[5] attributed this to the difference in metabolic rate between youth and age. Measurement of the change of MAC with age made it possible to quantify this clinical impression. In 1996, Professor Mapleson[6] published an analysis of this change using data derived from a comprehensive search of the literature. He concluded that from the age of 1 yr onwards $\log_{10}$ MAC decreased with age at the same rate for all inhaled anaesthetics, and that the rate of decrease was 6% per decade of year of age. This finding is of theoretical importance and the magnitude of the change, particularly at the extremes of age, make it of great practical importance as well. The current paper, in this issue by Nicalls and Mapleson,[7] presents the findings of the 1996 paper in graphical form. It is produced in response to 'difficulty in estimating age related MAC for a patient in a clinical setting'. The difficulty referred to has two components and both are removed by these charts. One difficulty is the need for rapid calculation of the 6% change per decade. The other is allowing for the presence or absence of nitrous oxide, and the vertical scales on the graphs are calibrated for nitrous oxide 0, 50, and 67% in order to meet this point.

The MAC concept, or some equivalent measure of anaesthetic potency, became necessary when the use of paralysing agents entered routine anaesthetic practice.[8] During inhalation anaesthesia before this event, the monitoring of depth of anaesthesia was an automatic and continuous process. If the patient became too light he moved, if too deep then respiration became impaired. The anaesthetist exercised his craft in maintaining the optimum equilibrium between these two boundaries. The detection of the two boundaries depended on observation of muscular activity. If this was blocked then new ways of defining the safe boundaries of the anaesthetic state were needed. It became necessary to know the concentration of agent required to ensure anaesthesia.

If the anaesthetized, unparalysed patient does not move on incision it is safe to assume that anaesthesia is deep enough. That is to say that as well as not moving, the patient will have no subsequent memory of surgery. In the extensive literature on this subject, only one case has been recorded[9] in which it seems beyond doubt that an unparalysed patient spontaneously breathed a measured mixture of nitrous oxide and halothane without moving or

showing other signs for a long orthopaedic procedure, and had some memory of the conversation in the operating theatre. There was no complaint of pain.

The MAC concept has proved very fruitful; it supports Meyer and Overton in correlating closely with lipid solubility and this correlation extends over a very wide range. In 1994, it was established[10] that MAC was independent of cerebral function and was determined at spinal (motor neurone) level. This correlated with the impression of experienced anaesthetists that cerebral concentrations of less than 1 MAC were sufficient to abolish consciousness. These conscious blocking concentrations (designated as MAC awake or MAC_{aw}) are not so easy to determine as the classical movement blocking MAC. This is because the end-point conscious/unconscious is less clearly defined than move/not move. For this reason, MAC_{aw} is at present best presented as a fraction of MAC, which has been so well studied. It has been shown that for isoflurane and sevoflurane, MAC_{aw} decreases with age at the same rate as does MAC.[11]

In 2001, Professor Eger published[12] a further comprehensive review of MAC determinations with conclusions closely similar to those of Mapleson. This review also considered data on MAC_{aw}, which was first described in 1970.[13] It was defined as the alveolar concentration of agent which was midway between that permitting response to command and that preventing it. Each alveolar (end-tidal) concentration was recorded after a 15-min period of constant alveolar concentration maintained by controlled ventilation (slow washout). This was done to ensure equilibrium between the alveolar and brain concentrations of agent. The finding was that MAC_{aw} was 0.5–0.6 of MAC but that when patients were allowed to awake breathing air spontaneously (fast wash-out) then considerably lower values were obtained. This difference was attributable to failure of equilibration between brain and alveolus. The agents studied were all of high solubility and this source of error should be reduced with modern agents. Eger concludes that for desflurane, isoflurane, and sevoflurane, MAC_{aw} is one-third of MAC. This figure is clearly of clinical importance.

The Eger review[12] gives a figure, derived from animal work, of a 4–5% decrease in MAC with each degree decrease in body temperature for the potent inhaled agents. Such a change can be at least partly explained by solubility changes with temperature but the failure to find such changes for nitrous oxide lacks explanation.

Another interesting MAC variant is MAC_{bar}. This was first described in 1981,[14] and is defined as the brain concentration of agent, which blocks adrenergic responses to skin incision. The responses studied are typically increases in heart rate and arterial pressure. The first paper concluded that MAC_{bar} for halothane was 1.45 MAC. Other workers[15] have found MAC_{bar} for desflurane and isoflurane to be 1.3 MAC (SD 0.34), but for sevoflurane a figure of 3.5 MAC (SD 0.2) has been given.[16]

Although there are considerable variations in MAC_{bar} as a fraction of MAC, there is no doubt about the great reduction in MAC_{bar} by opiates. MAC is also decreased. Typical results for studies on this subject[14] show a MAC_{bar} of 1.3 MAC for isoflurane and desflurane reduced to 0.55 and 0.40 MAC, respectively, by fentanyl 1.5 $\mu g\ kg^{-1}$. This effect is the basis for the routine use of opiates in modern anaesthesia. Doubling the dose of fentanyl produced no further reduction of MAC_{bar} and this demonstrates another feature of opiate use during anaesthesia. There is a ceiling effect; quite a modest dose of opiate produces a big reduction in MAC_{bar} but thereafter, however big a dose of opiate is given, there is no further decrease in MAC_{bar}. There appears to be an irreducible minimum of anaesthetic agent required for anaesthesia. Opiates alone cannot produce anaesthesia whatever the dose. A finding complementary to this is that although opiates do reduce MAC_{aw}, they do not do so to such a great extent as they do to MAC_{bar}, and there appears to be a ceiling effect here. A final conclusion from these MAC observations is that for practical purposes, inhalation agents can be regarded as additive in their actions although different kinetics, attributable to different solubilities, may obscure this fact.

The foregoing has been an attempt to show areas of interest, which become accessible when age-compensated MAC for each patient is easily available. Indeed, age-compensated MAC may in future be displayed on the anaesthetic agent monitor during every anaesthetic.

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