How Much Anesthetic?

Understanding cellular and molecular mechanisms in illness has become a necessity for effective treatment of disease. Advances in management of patients depend increasingly on a substratum of knowledge gained in simpler systems, and current research on the hazards of anesthetics identified at the cellular level amply testifies that the practice of anesthesiology is no exception.

It is true that the artificiality and simplifications of in-vitro studies sometimes outrage clinicians accustomed to wrestling with the baffling complexities of the whole organism. Yet it is clear enough that in order to understand how the cells of the body work together in groups it is necessary to understand how they behave as individuals. There is thus good reason to bring tissue culture techniques into the anesthesiology laboratory, as Corssen and Allen1 did to such good effect, to study isolated cells in the presence of anesthetic drugs at clinical or even at potentially toxic concentrations. The suspension cultures described by Jackson and Epstein in this issue and the monolayer cultures employed by others are further cases in point. Well executed basic work would interest the general medical reader more often if he had less difficulty in relating the drug levels used by experimenters to the drug levels present in anesthetized patients. Clinical drug concentrations generally are given as milligrams per milliliter, but investigators trained to think in terms of molecules prefer to express concentration as the number of molecules per liter, e.g., one millimole per liter, or $6.02 \times 10^{23}$ molecules per liter. They might communicate to better advantage if they adopted the practice of presenting their data in alternative units also. The statement that 50 per cent inhibition of cell growth requires $8 \times 10^{-4}$ M amobarital is apt to be lost on a physician until he discovers that this means about 200 mg per liter, or 20 mg/100 ml. He can then appreciate that the level under consideration is about twice the level encountered in the plasma during deep barbiturate coma.

Somewhat paradoxically, with volatile anesthetics mg/100 ml is less satisfactory for the statement of levels in blood or culture medium. The anesthesiologist doses these drugs as vapors, that is to say, as partial pressures (in torr or fractions of one atmosphere), and cannot translate mg/100 ml into pressure without knowing the solubility in the non-gaseous phase. A case could be made for always mentioning the relevant distribution coefficient when a level of volatile anesthetic is cited as mg/100 ml. But the same objective, an intelligible expression of the anesthetic level is attainable through an extension of the MAC concept developed by Eger2 and his associates: the minimum alveolar anesthetic concentration needed to abolish visible reaction to a surgical incision. A major merit of MAC is that it draws attention to the level of volatile anesthetic inside the body, rather than to the concentration delivered by the anesthesia machine. As such, it has contributed new objectivity to the thinking of anesthesiologists and has been quickly assimilated into practice.

So useful an idea was almost bound to be tried out in ways for which it was not designed, and some of these errors have been pointed out by Waud and Waud.3 Now its extension to in-vitro studies, for example, to the culture medium of hepatoma cells, as elsewhere in this issue, points up a further hazard. Correlation of the level in a liquid or tissue phase with the concentration of anesthetic gas in the lungs is difficult when these are expressed in different units. The clinician needs a way of expressing all volatile anesthetic levels, whether in vivo or in vitro, in the same familiar units. He can do this without effort simply by stating all such levels as partial pressures, regardless of phase. Pressure units are just as applicable in the blood and brain as in the alveoli and allow direct comparison between the various body phases. To take an example, the minimum alveolar anesthetizing pressure (MAP) of halothane, about $0.8 \text{ atm} \times 10^{-2}$ (0.8 hundredths of one standard atmosphere),

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is probably only a little higher than the minimum cerebral anesthetizing pressure, whereas the respective concentrations, about 6 and 14 mg per 100 volumes, respectively, diverge considerably. Essentially, the proposal is to present MAC in a form applicable to the blood and tissues as well as the alveoli, to detach the MAC numbers from units of concentration and attach them to units of pressure, namely, "per cent of one standard atmosphere." Unlike torr, this pressure unit enables one to leave the numerical values unaltered and to contrast measurements in other phases directly with the anesthetizing concentration in the alveoli.

This stratagem is possible because the original MAC measurements were made virtually at sea level, so that the MAC value and its corresponding MAP value expressed as "per cent of one standard atmosphere" are numerically the same. Of course, at higher altitudes MAC (a concentration) would increase but the minimum alveolar anesthetizing pressure would not.

To think and speak in terms of volatile anesthetic pressures, instead of concentrations, does not involve learning any new numbers, and makes for reader understanding of levels in unfamiliar phases. It rationalizes terminology, reduces the burden on memory, and, not least, respects the thermodynamics of the system, since difference in pressure and not difference in concentration is the force that drives volatile anesthetic molecules across phases.

In general, anesthetic levels in unfamiliar phases such as culture media become meaningful to the clinician only when they are presented in the same units as those he uses in administering the drugs to patients.

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References

Drugs

PROPOXYPHENE HYDROCHLORIDE A review of the published literature on propoxyphene hydrochloride was undertaken to determine if the wide popularity of the drug is justified. Twenty double-blind studies were reviewed in a bibliography of 243 articles. The addiction liability of propoxyphene is low but several reports have demonstrated the abuse potential of the drug. The analgesic action of propoxyphene is not superior to that of codeine or aspirin. No definite statement about the relative incidences of side-effects can be made. (Miller, R. R., and others: Propoxyphene Hydrochloride, A Critical Review, J.A.M.A. 213: 996 (Aug.) 1970.)

PANCURONIUM Pancuronium is an amino-steroid neuromuscular blocker whose activity appears to be localized to the neuromuscular junction. It is a nondepolarizing relaxant with medium to long action and low toxicity, and is free of undesirable side-effects. It has little or no effect on the cardiovascular system and does not cause bronchospasm. It is easily reversed by neostigmine. The author uses it "sandwiched between the test dose of thiopentone and the sleep dose." Intubation is said to be easy and no "bucking" is seen. (Wilson, D. S.: Pancuronium, Der Anaesthesist 19: 169 (May) 1970.)