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Editorial Views

Anesthetics and Cell Division

IN CELLULAR BIOLOGY particular interest is focused on the events that trigger mitosis. Duplication of deoxyribonucleic acid (DNA) is followed by mitosis (M), which is followed again by DNA synthesis (S). Two periods (G_I and G_{II}) of varying length occur between M and S. We do not understand what happens during G_I and G_{II}, because we have not been able to associate them with any specific activity. The triggering event is not known, but the most attractive hypotheses[1] suggest: that 1) cell division takes place when cellular dry mass has reached a critical level; 2) the nucleus controls growth and protein synthesis through ribonucleic acid (RNA) synthesis and transfer; 3) RNA synthesis parallels the amount of DNA present; 4) nuclear division, or separation of the chromatids, is the chief event initiating the increased rate of growth. Accordingly, the generation cycle of a cell is a continuum, and a delay in one phase may, for instance, be the result of a specific pharmacologic effect in the one or in a completely different phase.

In this issue of the Journal, in an interesting study by Bruce and Traurig, the anesthetic effect on the duration of the generation cycle of one group of cells is explored. The authors conclude that halothane in low clinical concentrations specifically prolongs a mammalian cell generation cycle *in vivo*. This conclusion is valid provided halothane does not delay or prolong uptake and distribution of ^{3}H-thymidine, or decrease the transport of this precursor across the cell membrane. Labeling of the mitotic nuclei to the 80 per cent level rather than saturation might render the method more sensitive and provide additional information in this area. The data, unfortunately, do not permit further conclusions.[2] In order to determine the duration of each phase in the cycle by ^{3}H-thymidine labeling, it is necessary to count labeled nuclei in interphase as well as mitosis, and to characterize the slope of the initial ascending limb of the "pulse-labeling" curve with observations every 15 minutes. As a matter of fact, the percentage of labeled mitotic figures at one hour with 0.5 per cent halothane appears to be significantly smaller than that in the control group (table 1) suggesting that halothane prolonged the replacement of unlabeled with labeled mitotic figures. To detect an effect on one of the intramitotic phases, it is necessary to count the mitoses in each phase. Although the study may raise more questions than it answers, it is in itself an important contribution in an area that obviously deserves further study.

A few studies in rodents and the chicken embryo indicate that anesthetics are weak teratogens.[3] The question is: where is the site of action? Do anesthetics arrest mitosis in metaphase as reported by a number of investigators,[4] or do anesthetics interfere with the synthesis of DNA? We do not know, but the two possibilities need not be incompatible. We do not even know if mitotic changes and teratogenicity are related. Anesthetics affect mem-

brane permeability and transport, and could deprive the embryo of sufficient nutrients at a time when development is particularly rapid. Mitotic inhibition, on the other hand, may lead merely to cell death and not appear as a subsequent malformation. Until a relationship has been established, we shall have to keep open minds and be willing to consider mitotic changes and teratogenic effects as unrelated phenomena.

We now know that pharmacologic agents may affect a series of receptor sites in the cell. Thus, narcosis is only one of several cellular effects of anesthetics.[5] Others include decreased contractile force, inhibition of metabolism, interference with mitosis, and teratogenicity. All these effects occur with concentrations used clinically. In the intact animal convulsions or irreversible cell damage are unpredictable complications frequently seen with higher concentrations. We do not know the sort or number of receptor sites involved; therefore, there is a great need for more information about all anesthetic effects. Ultimately, we should be able to take cellular effects such as described by Bruce and Traurig into consideration in clinical practice, because all cellular actions must somehow influence the course of any anesthetic procedure.

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