These results suggest that amidephrine activates glycogen phosphorylase by an α-receptor mediated mechanism not associated with a rise in the intracellular level of cyclic AMP.

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Cyclic AMP in HeLa cells stimulated with cholera enterotoxin and methylxanthines

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There are two general approaches being used to elucidate the regulatory role of cyclic AMP in cell growth. One is to add cyclic AMP or its analogues to the system under study and observe its effects upon various parameters of cell activity. The other approach is to alter the intracellular levels of cyclic AMP by modulation of adenyl cyclase or phosphodiesterase activity. We report here our attempts to manipulate endogenous cyclic AMP in cells in tissue culture.

HeLa cells were grown in suspension culture in Jokliks medium containing 7% calf serum to a density of 8×10^5 cells/ml. Cyclic AMP levels were measured as described previously (Albano, Barnes, Maudsley, Brown & Ekins, 1974). In cells incubated in the presence of 8 mM theophylline cyclic AMP levels were increased by cholera enterotoxin (1 μg per 10^6 cells) but not by prostaglandin E_1 (10 μg) or adrenaline (10 μg). In the absence of theophylline, toxin produced little or no increase in cyclic AMP. A characteristic of toxin stimulation of cyclic AMP is the existence of a lag period between the addition of the toxin and the increase in cyclic AMP (Pierce, Greenough & Carpenter, 1971). In HeLa cells the lag period is of 5-10 min duration which is much shorter than it is for several other systems such as adrenal cells (Haksar, Maudsley & Péron, 1975).

Theophylline alone in concentrations up to 32 mM or 3-isobutyl-1-methylxanthine in concentrations up to 2 mM did not increase the basal levels of cyclic AMP. These concentrations of theophylline and 3-isobutyl-1-methylxanthine, however, did reduce the uptake of [^{3}H]-leucine. Caffeine had similar effects and of the agents used 3-isobutyl-1-methylxanthine was the most potent and caffeine the least active. Thus, while the relative potencies of the methylxanthines approximate their known ability to inhibit cyclic nucleotide phosphodiesterases the effects upon transport may not be mediated by cyclic AMP. In this system, therefore, methylxanthines do not appear to be useful for the manipulation of basal cyclic AMP levels. Furthermore, these results also indicate that in HeLa cells cyclic AMP produced in response to toxin is turned over more rapidly than cyclic AMP in the resting cell.

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