energy electrons of the redox system and high-energy phosphate bonds in ATP are closely coupled. Therefore the specific determination of an intermediary compound between two such enzymes in a structurally organized system may be a direct way of measuring the interactions (Jardetzky, 1966) and the related permeability properties occurring within the membrane itself.

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The Effects of Theophylline on Mucosubstance Secretion by Rous Sarcoma Cells

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Cell cultures of rat submaxillary gland maintain the secretion of mucosubstances for many months (Gallagher & Marsden, 1969). The rate of secretion is stimulated 28% ($P < 0.02$) by 0.1 mM-adrenaline and 111% ($P < 0.001$) by vasopressin (0.5 i.u./ml.). Similar observations have been made on mucosubstance release by Rous sarcoma cells.

The action of both adrenaline and vasopressin is believed to involve cyclic AMP (adenosine 3':5'-cyclic monophosphate) (Robison, Butcher & Sutherland, 1968).

At 5 mM the dibutyryl derivative of cyclic AMP stimulates the secretion of mucosubstances by Rous sarcoma cells nearly threefold. Derivatives of cyclic AMP have also been found to stimulate secretion in rat parotid gland (Babad, Ben-Zvi, Bdolah & Schramm, 1967) and in rabbit pancreas (Ridderstrap & Bonting, 1969), and in both cases stimulation could also be achieved with theophylline, which, by inhibiting phosphodiesterase, elevates the concentrations of endogenous cyclic AMP (Humes, Rounbehler & Kuehl, 1969). In Rous sarcoma cells, however, 5 mM-theophylline caused a marked inhibition (47%; $P < 0.1$) of mucosubstance release; only at lower concentrations (1.7 mM) was a stimulation (68%; $P < 0.1$) noted. Thus the effect

of theophylline appears to involve rather more than simple inhibition of the breakdown of cyclic AMP.

Theophylline has been found to inhibit protein synthesis in rat adrenal gland (Halkerston, Feinstein & Hechter, 1966), and we have found that puromycin at a concentration of 100 μ g/ml inhibits virtually completely the incorporation of D-[1- 14 C]-glucosamine into mucosubstances by cell cultures; a similar effect on the synthesis of exportable protein by cycloheximide has been reported for guinea-pig pancreas (Jamieson & Palade, 1968). These observations suggest that the use of theophylline to mimic the effects of cyclic AMP should be approached with caution where additional protein synthesis may also be involved.

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The Transformation of Lymphocytes by Adenosine 3':5'-Cyclic Monophosphate, and Consequent Changes in Histone Microstructure

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Cyclic AMP (adenosine 3':5'-cyclic monophosphate) will transform thymocytes (MacManus & Whitfield, 1969) at concentrations in the range 0.01–1.0 μ M. At 0.1–10 μ M no stimulation of human lymphocytes by cyclic AMP was observed (Hirschhorn, Grossman & Weissmann, 1970). In contrast with this it is reported here that cyclic AMP at a concentration of 0.01–0.1 μ M will stimulate cultures of lymphocytes prepared from pig peripheral blood as described by Forsdyke (1968). The timing and extent of the initial polydisperse RNA synthesis (0–1 h), subsequent rRNA synthesis (4–5 h) (Monjardino & MacGillivray, 1968), eventual DNA synthesis (approx. 72 h) and mitosis (approx. 90 h) are identical for cyclic AMP and phytohaemagglutinin. Chlorpromazine at a concentration that is reported to inhibit the adenylate cyclase membrane system (Wolff &