THE INABILITY OF DIBUTYRYL ADENOSINE 3',5'-MONOPHOSPHATE TO INDUCE THE DECIDUAL REACTION IN INTACT PSEUDOPREGNANT MICE

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The technique for assessing the ability of a compound to initiate the decidual response is simple and conclusive. It involves introducing the compound in solution into the uterine lumen of an intact rat or mouse during the 'sensitive period' of pseudopregnancy (Finn & Keen, 1963; Hetherington, 1968). This technique was used to compare the ability of arachis oil, phosphate-buffered saline (PBS; Dulbecco & Vogt, 1954) and dibutyryl adenosine 3',5'-monophosphate (dibutyryl cyclic AMP—dcAMP) to initiate the decidual response after injection into the uterine lumen of the mouse at various times on the 4th day of pseudopregnancy.

Pseudopregnancy was induced in A2G mice from a closed colony in the Department, by mating them with vasectomized males of the same strain, vaginal plugs being taken to indicate the 1st day of pseudopregnancy. Animals were allocated to fifteen groups, each comprising four to seven mice. On the 4th day at 09.30, 12.30 or 15.30 hours, a single intraluminal injection (by way of the uterotubal junction) of 0.02 ml arachis oil, PBS or a solution of dcAMP (Sigma) in PBS was given. Three concentrations of dcAMP were used: 1.25 mM, 2.5 mM and 3.75 mM. At autopsy on the 7th day, the horns were excised, divided at the cervix and weighed separately before being fixed in Bouin's solution for subsequent histological examination.

A decidual response was observed in six of seven horns treated with arachis oil at 12.00 hours and one of five horns receiving oil at 09.30 hours. The mean weight of the horns with deciduomata was 111.0 mg, which was significantly different from the mean weight of the contralateral horns without deciduomata (46.5 mg). There was no evidence of a decidual reaction in any of the mice receiving oil at 15.30 hours. The PBS was unable to induce the response, a finding which agrees with those of Finn (1965). None of the three concentrations of dcAMP at any of the times of injection was able to induce deciduomata. The mean weights of the horns injected with dcAMP did not differ significantly from those of the respective contralateral horns, and varied between 29.6 mg and 42.5 mg. It was concluded that dcAMP was unable to induce the decidual response in these mice.

Histamine has been suggested as the stimulus for the decidual response in rodents (Shelesnyak, 1960). This theory has not won universal acceptance (see

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Finn, 1971) and was later modified by Shelesnyak, Marcus & Lindner (1970) to give histamine the rôle of mediator in the action of the inducing stimulus. The exact nature of the stimulus remains unknown (McLaren, 1969, 1970). Histamine is known to exert its action by stimulation of adenylyl cyclase (Rall & Kakiuchi, 1966) and, in common with other compounds whose action is mediated by this enzyme, it should be possible to mimic the effects of histamine by administration of exogenous cyclic AMP (Robison, Butcher & Sutherland, 1971). The inability of the dibutyryl analogue of cyclic AMP, which is known to be more potent than the pure form (Posternak, Sutherland & Henion, 1962), to initiate the decidual response suggests that histamine is not involved in the response either as a stimulus or as a mediator of the stimulus. This result also suggests that whatever is the stimulus, it is unlikely that it exerts its effect by stimulating adenylyl cyclase in uterine cells. Leroy, Vansande, Shetgen & Brasseur (1974) have reported that dcAMP injected intraluminally does not induce the decidual response in mice which have been primed with hormones after long-term ovariectomy. Some deciduomata were obtained after intraperitoneal injection of dcAMP and theophylline, but the dose of the nucleotide, and mortality of the mice, was extremely high.

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