[6] Haynes, jun., R. C., *J. Biol. Chem.*, **233**, 1220 (1958).
[7] Grahame-Smith., D. G., Butcher, R. W., Ney, R. L., and Sutherland, E. W., *J. Biol. Chem.*, **242**, 5535 (1967).
[8] Haynes, jun., R. C., Koritz, S. B., and Peron, F. G., *J. Biol. Chem.*, **243**, 1421 (1959).
[9] Ney, R. L., *Endocrinology*, **84**, 168 (1969).
[10] Friedman, S., and Kaufman, S., *J. Biol. Chem.*, **240**, 4763 (1965).
[11] Viveros, O. H., Arqueros, L., and Kirshner, N., *Life Sci.*, **7**, 609 (1968).
[12] Axelrod, J., *J. Biol. Chem.*, **237**, 1657 (1962).
[13] Nagatsu, T., Levitt, M., and Udenfriend, S., *J. Biol. Chem.*, **239**, 2910 (1964).
[14] Landsberg, L., and Axelrod, J., *Circulation Res.*, **22**, 559 (1968).

Induction of Cleft Palate in Rats with Intra-amniotic Corticoids

TESTS of teratogenicity using tissue culture, laboratory rodents or primates may not yield results applicable to man[1]. Different species and even strains differ in their response to teratogens. In mice, the percentage induction of cleft palate after administration of corticoids varies from strain to strain[2]; in rats, the effect cannot be found at all[3–5]. The relative influences of maternal metabolism on the one hand, and of specificity of the morphogenetic processes in the embryo on the other, remain unknown. The development of a test for the teratogenic effect of drugs depends on the solution of this problem: strict species specificity of the embryonic morphogenetic mechanisms would absolutely preclude extrapolation from laboratory animals to humans.

Administration of the substance to be tested directly into the amniotic sac of the embryo eliminates the influence of the maternal metabolism and of the placental barrier. We have therefore administered corticoids by this route, as described by Dostál[6], to determine whether the resistance to cleft palate in rats is a function of the embryo or the mother.

Wistar–Konárovice embryos were used. Doses of 0.2, 0.4 or 0.6 mg of soluble hydrocortisone (Spofa) dissolved in 3 μl. of Ringer solution were injected into the amniotic sac on embryonic day 13, 14, 15 or 16. The results of the examinations on day 18 of embryonic development are presented in Table 1. After a single administration of various doses of hydrocortisone into the amniotic sac on day 14, 15 and 16 respectively the occurrence of cleft palate (CP) or of partial cleft palate (CPP)[7] was recorded in twenty-one of forty-five embryos. Administration of an inert vehicle to forty-seven embryos in the same experimental conditions failed to produce any malformations of this type (Z. Rychter, R. J. and O. Marhan, in preparation).

Thus it can be concluded that hydrocortisone can induce cleft palate in rat embryos, provided that it is administered beyond the placental barrier. This shows that the difference between the sensitivity of mouse and rat embryos to the teratogenic action of corticoids administered to pregnant animals should be sought in the transport channel before the placental barrier. It is not our aim to advance hypotheses about the possible causes of this resistance, but rather to draw attention to the value of intra-amniotic administration for the screening of drugs for teratogenic activity.

This experiment was initiated in Konárovice in cooperation with RNDr. O. Marhan.

MIROSLAV DOSTÁL
RICHARD JELÍNEK

Laboratory for Plastic Surgery,
Czechoslovak Academy of Sciences,
Prague 2, Legerova 61

Received November 23, 1970.

[1] Warkany, J., in *Congenital Malformations* (edit. by Fraser, F. C., and McKusick, V. A.), 378 (Excerpta Medica Foundation, Amsterdam and New York, 1970).
[2] Fraser, F. C., Kalter, H., Walker, B. E., and Fainstat, T. D., *J. Cell. Comp. Physiol.*, **43**, Suppl. 1, 237 (1954).
[3] Csaba, G., Törö, I., and Fischer, J., *Acta Paediat. Acad. Sci. Hung.*, **8**, 217 (1967).
[4] Angerwall, L., and Lundin, P. M., *Endocrinology*, **74**, 986 (1964).
[5] Kendrick, F. J., and Feild, L. E., *Anat. Rec.*, **159**, 353 (1967).
[6] Dostál, M., *Teratology* (in the press).
[7] Dostál, M., and Jelínek, R., *Folia morphol.*, **19**, 88 (1971).

Central Visual Discharge Time-locked with Spontaneous Eye Movements in the Cat

IT is well known that there is an illusory displacement of the visual field in man when the eyes are moved passively, while active movement of the eyes results in a stable perception. The existence of a central neural mechanism as part of the excitation pattern of the overt movement has been postulated in an attempt to account for these phenomena[1,2].

Any efferent discharge, resulting in an ocular movement, would be accompanied by a concurrent central discharge into the visual system, the effect of which would be to "anticipate" and "counteract" those changes in afferent stimulation which result from the movement of the eyes (the "corollary discharge" of Sperry[1]). Such a self-regulating compensatory mechanism would enable a constant visualized environment in normal conditions of active displacement of the eyeballs. If the eyes were moved passively, however, no concurrent central discharge would take place to compensate for the relative motion

Table 1 Induction of Cleft Palate in Rat Embryos

Day number and dose		Treated embryos: Normal No.	%	CPP No.	%	CP No.	%	Dead No.	%	Dead No.	%	Untreated embryos: CP No.	%	CPP No.	%	Normal No.	%
13																	
0.2 mg	5	17	77.3	1	4.5	0	0	4	18.2	2	8.7	0	0	0	0	21	91.3
14																	
0.2–0.4*	4	1	7.1	6	42.8	5	35.7	2	14.3	0	0	0	0	0	0	20	100.0
15																	
0.6 mg	5	2	12.5	3	18.7	3	18.7	8	50.0	0	0	0	0	0	0	12	100.0
16																	
0.6 mg	4	10	66.7	3	20.0	1	6.7	1	6.7	0	0	0	0	1	6.7	14	93.3

Hydrocortisone soluble Spofa injected into amnion of Wistar–Konárovice rats. Controls were taken from the opposite horn of the same female.
* Ten embryos were injected with 0.2 mg, four embryos with 0.4 mg.

© 1971 Nature Publishing Group