

## Carcinogenic Activity of Aliphatic Nitrosamines Via the Mother's Milk in the Offspring of Syrian Golden Hamsters (35416)

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(Introduced by P. Shubik)

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Certain nitroso compounds studied in hamsters have been found to cause tumors mainly in the respiratory tract (1). Diethylnitrosamine (DEN) also had a transplacental carcinogenic effect in hamsters (2). When the litters of treated and untreated mothers were exchanged, tumors were found only in the offspring of carcinogen-treated mothers nursed by untreated mothers. The offspring of untreated mothers nursed by mothers treated with carcinogen until the end of pregnancy showed no neoplastic alterations in the respiratory tract (3). We were able to show the presence of nitroso substances in the placenta and fetus of treated pregnant hamsters. Therefore, it was assumed that under these conditions, little or no carcinogen reached the young via the milk after delivery. In the experiments reported here, the effect on the young of carcinogen administered to mothers during lactation was studied.

*Materials and Methods.* In this set of experiments, 6-month-old hamsters were treated with high doses of DEN or dibutyl nitrosamine (DBN) 1 to 30 days after delivery. Three groups of five animals received sc administrations of 5, 10, and 20 mg/kg of body weight of DEN dissolved in water. Three other groups received 300, 600, and 1200 mg/kg of body weight of DBN in olive oil (Table I).

*Results.* Nearly one-third of the offspring in the DEN groups died while nursing, showing acute toxic alterations in the liver and kidney. These changes were not observed in the DBN groups or in the controls. The experiments are still underway, with approximately 50% of the young still living more

TABLE I. Treatment During Lactation Period.

DEN (mg/kg of body wt)	5	10	20
Treated mothers	5	5	5
Offspring surviving at day 28	14	25	15
DBN (mg/kg of body wt)	300	600	1200
Treated mothers	5	5	5
Offspring surviving at day 28	21	35	30
0.9% NaCl (ml/kg of body wt)	10	Olive oil (ml/kg of body wt)	10
Treated mothers	5		5
Offspring surviving at day 28	31		29

than 1 year after the treatment of their mothers.

Focal hyperplastic and dysplastic alterations of the mucosa in the trachea and nasal cavity were seen in treated mothers. All mothers also had tracheal papillary tumors. The latent period for these tumors was 8 weeks for DEN- and 24 weeks for DBN-treated hamsters, the same values found in nonpregnant adults (4). In addition, DEN-treated mothers showed papillary tumors in the nasal cavity. Papillary tumors also developed in the trachea (Fig. 1) and nasal cavities of the young of both DEN- and DBN-treated mothers (Table II). Most of these tumors have been found in the highest

TABLE II. Tumors in Treated Mothers and Offspring.

		Tracheal papillomas	Nasal cavity tumors
DEN	Mothers	11/15	6/15
	Offspring	12/23	1/23
DBN	Mothers	11/15	0/15
	Offspring	5/18	0/18

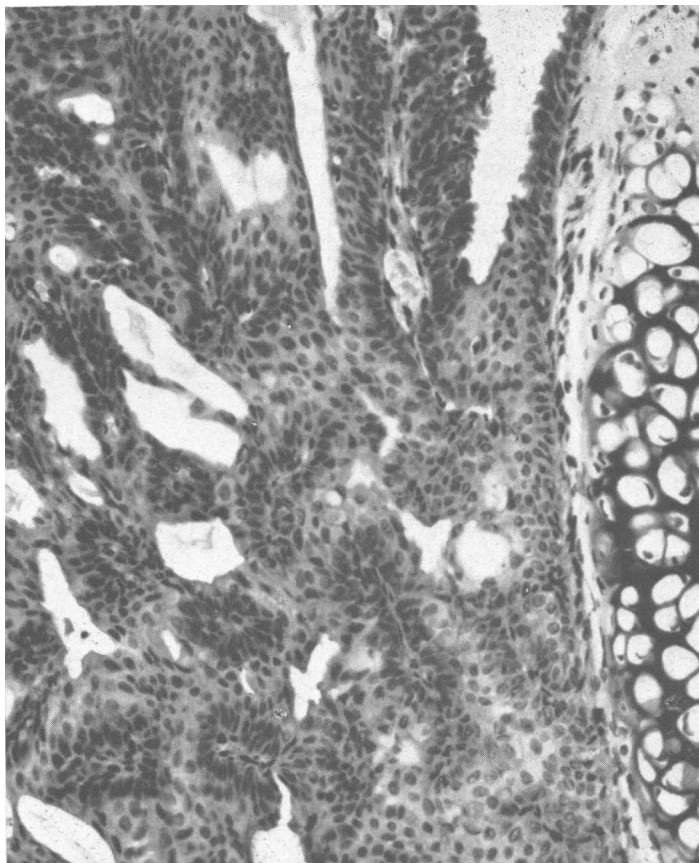


FIG. 1. Tracheal papillary tumor in offspring of mother treated with DEN during lactation ( $\times 170$ ).

dosage groups, seeming to indicate a dose-response effect. However, the latent period of tumor development in the DEN offspring was longer than in the mothers, while in the DBN group the reverse was true.

*Discussion.* Hyperplasia, dysplasia, and papillary tumors of the trachea appearing in the offspring of hamsters treated during pregnancy closely resemble the morphological patterns seen in other adults after application of various nitroso compounds (3, 5). The "organotropism" found in the diaplacental study was also seen in the present experiment. The development of papillary tumors in the trachea and nasal cavity of the young after treatment of their mothers during lactation indicates their exposure to the carcinogen or its metabolites. Although the possibility of exposure to carcinogen via mother's urine or

feces cannot be disregarded, the milk is most likely acting as the carrier. However, the presence of carcinogens in milk remains to be demonstrated. The properties of milk as an emulsion of lipid- and water-soluble substances make it particularly suitable as a vehicle. The placenta and the lactating mammary gland seem to be media which allow the passage of carcinogens or their effective form. The metabolites might be generated either within the placenta or milk-secreting epithelium.

These experiments suggest that a causative agent for tumor induction can be transmitted via placenta or milk, and give rise later to neoplasia in the young. Since the young are dependent on their mothers in both intrauterine and postnatal life, carcinogenic substances dangerous to the mother can

equally well endanger the young. We interpret these results as meaning that the testing of drugs only in adult, nonpregnant animals is inadequate as a safety precaution.

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1. Dontenwill, C., and Mohr, U., *Z. Krebsforsch.* 65, 166 (1962).

2. Mohr, U., Authaler, A., and Althoff, J.,

*Naturwissenschaften* 8, 188 (1965).

3. Mohr, U., Althoff, J., and Authaler, A., *Cancer Res.* 26, 2349 (1966).

4. Dontenwill, W., and Mohr, U., *Z. Krebsforsch.* 64, 305 (1961).

5. Herrold, K. M., *Proc. Amer. Ass. Cancer Res.* 5, 26 (1964).

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