Adv. Cancer Res., 1970, 30, 2796), the other a renal adenocarcinoma. The dose response for total tumour incidence is a probit curve.

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THE DEVELOPMENT OF TUMOURS IN A FEMALE RAT AND HER OFFSPRING, FOLLOWING ADMINISTRATION OF DIETHYLNITROSAMINE TO THE MOTHER DURING NURSING.

R. Schoental and E. C. Appleby. Department of Pathology, The Royal Veterinary College, London.

Several workers have demonstrated acute and chronic effects in rats suckled by mothers treated with toxic and carcinogenic substances such as pyrrolizidine alkaloids, cycasin, bracken etc., but no information was available with regard to the effects of diethylnitrosamine.

We administered this substance to 3 female rats nursing their young. One mother given 7 doses died after 9 months and had a kidney tumour; nasal and other tumours started to appear among her offspring from the 10th month of life.

Recently, Mohr et al. (Z. Krebsforsch., 1972, 78, 72) reported nasal and respiratory tract tumours in golden hamsters, among the offspring and mothers treated with diethylnitrosamine during nursing.

Besides the parent nitrosamine, milk may contain in addition some of its biologically active metabolites. N-ethyl-N-nitrosacetalddehyde has been suggested as one of the possible active intermediates in the carcinogenic action of diethylnitrosamine.

POTENTIAL ALKYLATING AGENTS FROM THE OXIDATION OF CARCINOGENIC CYCLIC N-NITROSAMINES. B. C. Challis and M. P. Rayman. Chemistry Department, Imperial College, London.

Carcinogenesis by some secondary N-nitrosamines may arise (Magee and Barnes, Adv. Cancer Res., 1967, 10, 163) from their alkylating action after metabolic oxidation of the α-carbon atom and subsequent decomposition to a diazo derivative (equation). The validity of this hypothesis is apparently questioned by the properties of cyclic N-nitrosamines (e.g. N-nitrosopiperidine) that are potent carcinogens yet chemically inert.

We have shown, however, that N-nitrosopiperidine is oxidized by a model microsomal system (Udenfriend et al., J. Biol. Chem., 1954, 208, 731) to N-nitroso-4-piperidone plus other products. This oxidation followed by ring cleavage is suggested as a mechanism whereby alkylating species could be generated.

INHIBITION OF METABOLISM AND TUMORIGENESIS OF 15,16-DIHYDRO-11-METHYL-CYCLOPENTA[A]PHENANTHRENE-17-ONE BY 7,8-BENZFLAVONE. M. M. Coombs and C. W. Vose. Imperial Cancer Research Fund, Lincoln's Inn Fields, London.

A number of cyclopenta[a]phenanthrenones have been tested for carcinogenic activity (Coombs and Croft, Prog. exp. Tumor Res., 1969, 11, 69).

The 11-methyl-17-ketone is a potent carcinogen for mouse skin. This ketone is metabolized by microsomal mixed function oxidases and binds covalently to DNA in vitro in the presence of rat liver microsomes.

7,8-Benzflavone, an inhibitor of the microsomal enzymes, inhibits covalent binding of the ketone to DNA at a 3:1 molar ratio of benzflavone compound. When 7,8-benzflavone is painted simultaneously with the ketone on mouse skin, suppression of the carcinogenic action of the ketone results. Thus metabolism of this ketone is required to cause in vitro binding to DNA and for its tumorigenic activity.

HYDROCARBON - DEOXYRIBONUC - LEOSIDE PRODUCTS FORMED BY THE BINDING OF DERIVATIVES OF 7-METHYLBENZ[A]ANTHRACENE TO DNA. W. M. Baird, A. Dipple, P. L. Grover, P. Sims and P. Brookes. Chemical
Carcinogenesis Division, Chester Beatty Research Institute, London.

Hydrocarbon-deoxyribonucleoside products present in the DNA of mouse embryo cell cultures that had been treated with [3H]-7-methylbenz(a)anthracene were isolated from enzyme digests of the DNA by Sephadex LH20 column chromatography. Similar digests were prepared from DNA reacted in solution with either 7-bromomethylbenz(a)anthracene or the K-region epoxide of 7-methylbenz(a)anthracene and from DNA from cells treated in culture with either 7-hydroxy-7-methylbenz(a)anthracene, cis-5,6-dihydro-5,6 dihydroxy-7-methylbenz(a)anthracene, or the K-region epoxide of 7-methylbenz(a)anthracene. These digests contained no products identical with those obtained from hydrocarbon treated cells.

These results suggest that none of the above compounds is directly involved in the binding of this hydrocarbon to DNA.

THE TARGET CELL IN 7,12-DIMETHYLBENZ(A)ANTHRACENE CARCINOGENESIS IN THE MOUSE SUBMANDIBULAR GLAND IN VIVO AND IN VITRO. C. B. WIGLEY. Department of Cellular Pathology, Imperial Cancer Research Fund, Lincoln’s Inn fields, London.

Direct applications of a carcinogen (DMBA) on mouse submandibular gland epithelium in vivo and in vitro were compared. The granular tubule cell is the primary target cell in both systems. In vivo it shows degranulation, squamous metaplasia and increased DNA synthesis after 3–4 weeks. This is followed by the development of squamous carcinoma at 14–20 weeks. In vitro, untreated cultures show epithelial outgrowths which arise largely from granular tubule cells. These undergo a regeneration process in the explant before attachment to the substrate occurs.

Cultures in this regeneration phase were treated with DMBA at 0-1 μg/ml of medium. Approximately 10 weeks later foci of cells appear in some outgrowths which grow rapidly and have morphological features consistent with neoplastically transformed epithelium. Experiments are in progress to test the tumorigenicity of these cells.

STUDIES OF THE MECHANISM OF TUMOUR INITIATION. M. P. RAYMAN and A. DIPPLE. Chester Beatty Research Institute, London.

7 - Bromomethyl - 12 - methylbenz(a)anthracene is a more effective carcinogen than 7-bromomethylbenz(a)anthracene (Dipple and Slade, Eur. J. Cancer, 1971, 7, 473). Comparison of the products of reaction of each bromo compound with DNA in vitro and in vivo indicates that similar products are formed in each case through reaction on the amino groups of the DNA bases; that 7-bromomethyl - 12 - methylbenz(a)anthracene reacts less extensively with DNA than does 7-bromomethylbenz(a)anthracene; that no correlation exists between the amounts of any hydrocarbon-DNA product formed and carcinogenic potency; but that 7-bromomethyl-12-methylbenz(a)anthracene does exhibit a greater preference for attack on adenine residues in DNA than does 7-bromomethylbenz(a)anthracene. These findings do not support the view that DNA is the critical receptor for chemical carcinogens, unless the attack of these carcinogens on DNA exhibits a differential specificity for chromosomal sites which are specifically relevant to tumour initiation.

MITOTIC INHIBITION IN MAMMALIAN CELL CULTURES EXPOSED TO HYPERTONIC MEDIA. D. N. WHEATLEY. Department of Pathology, University Medical Buildings, Aberdeen.

An almost immediate cessation of mitotic division can be brought about by increasing the tonicity of the medium in cell cultures (Hughes, Quart. J. microsc. Sci., 1952, 98, 207; Stubblefield and Mueller, Cancer Res., 1960, 20, 1646). The effects of raising tonicity with Na+, K+, Li+, choline, urea and other substances will be discussed, particularly the ways in which they affect the flow of cells from G2 into mitosis as well as their action in mitosis itself. After an initial period of perturbation following treatment, cells adapt to the hypertonic medium (that is, within certain limits depending upon the substance used) and may begin to accumulate in metaphase. Several hours later some cells recover their ability to move out of metaphase into interphase.

One practical application of the accumulation of metaphases in hypertonic medium