in the experimental atrophy ('wasting syndrome') following neonatal thymectomy.

Concerning the pathological mechanism of these severe disturbances in the ossification process, the experimental data of PIERPAOLI and SORKIN are of interest[6]. They observed a marked degranulation of acidophilic cells in the anterior lobe of the pituitary after neonatal thymectomy in mice and postulated the existence of a thymus-hypophysis axis, possibly involving growth hormone. LAW et al. reported that in neonatally thymectomized and wasting mice the cells of the anterior pituitary exhibited a reduction in nuclear and cytoplasmic volume in comparison with control mice[7]. The thymic regression and the count and the nuclear volume of the acidophilic cells in the anterior lobe of the pituitary in atrophia infantum[4], and the control of enchondral ossification by somatotropic hormone are well known[8,9].

Taken together these data indicate the importance of the thymus and hypophysis for these osseal alterations. It appears a plausible supposition that the osseal changes are dependent on alterations produced by neonatal thymectomy and resulting in changes in the somatotropic hormone producing cells[10].

Zusammenfassung. In neonatal thymektomierten Mäusen wurden nach 6–7 Wochen röntgenologisch sowie histologisch das «wasting syndrome» und schwere Knochenatrophien beobachtet. Der Mechanismus der beobachteten enchondralen Ossifikationsstörung wurde diskutiert.

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Adrenal Lipid and Plasma Corticosterone Depletion after 7,12-Dimethylbenz(a)anthracene Administration to the Albino Rat

Mammary carcinoma may be induced in rats by the single feeding of the polynuclear aromatic hydrocarbon 7,12-dimethylbenz(a)anthracene (DMBA)[1]. Following administration of this compound necrotic changes occur in steroid hormone producing cells[2,3]. WONG et al.[3] have interpreted their results relative to tumor formation in terms of steric competition between carcinogen and steroid hormone. Thus, a depletion of steroid hormones brought about as a result of cellular necrosis has an enhancing effect on carcinogenesis by reducing the competitive inhibition on DMBA which would normally be exerted by the presence of these hormones. In order to test a portion of this hypothesis, i.e. depletion of steroid hormones we have measured the concentration of plasma corticosterone (CCS) in DMBA-treated animals. In this communication we wish to present the results of our investigations.

Materials and methods. Female Sprague-Dawley rats, 140–160 g, were obtained from a commercial supply house and maintained on laboratory chow and water ad libitum in appropriate animal quarters. At age 50 days, termed day 0, the experimental animals received, via stomach tube, 20 mg of purified DMBA dissolved in 1.0 ml of sesame oil. Control animals were given an equivalent amount of sesame oil in a similar manner.

On day 0, and for 6 consecutive days, blood for CCS determination was obtained by cardiac puncture and the plasma separated immediately by centrifugation. Plasma CCS was determined by a modification of the procedures of SILBER et al.[4] and GUILLEMIN et al.[5]. Plasma samples were pre-extracted with 3–5 volumes of petroleum ether and measured 1.0–3.0 ml aliquots were taken for analysis. The aliquots were extracted with 10.0 ml of dichloromethane. Following plasma aspiration the dichloromethane was extracted with the fluorescent reagent, sulfuric acid-ethanol, 3:1, V/V. This solution was transferred to matched cuvettes and read 30 min later in a Turner Fluorometer, Model 111, with a primary filter No. 47B and secondary filters Nos. 2A12 and 58. In order to be certain CCS was the steroid being measured the procedure was checked by various controls. Addition of known amounts of CCS to plasma was measured by the same technique as well as measurements of recovery from saline samples. Additionally, approximately 50,000 dpm of radioactive CCS was added to plasma samples, extracted, chromatographed in the Bush B_5 system[6] and scanned with a Vanguard Radiochromatogram Scanner for localization on the paper strips. Cold standards of several adrenal steroids were detected on these and parallel strips by their absorbance under UV-light at 240 μm.

Results. The data for plasma CCS levels of control and experimental animals are shown in the Table. Average values for the control animals, 15 μg/100 ml, remained unchanged throughout the period of the experiment. In the experimental series there was a rapid depletion of plasma CCS during the initial part of the experimental period. Recovery experiments with standard CCS showed our technique to be 85–92% efficient for the recovery of known amounts of crystalline steroid from rat plasma. Additionally, by the use of the ^{14}C-labeled CCS we found we could recover 90–94% of our starting material. Radiochromatographic analysis of the dichloromethane extracts

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showed the major area of radioactivity to be located in the same spot as 20 µg standard samples of CCS visualized with an UV-lamp. Some animals of each group were excited during handling and prior to and during cardiac puncture. Although blood samples from these animals were obtained and measured the results are not included in the data shown in the Table. The CCS values obtained from the control animals were, as expected, elevated when compared to their more quiescent littermates.

Discussion and conclusions. The major adrenal glucocorticoid of the rat is CCS[7–10]. Our measurements of the circulating plasma levels of this steroid show a decrease in plasma CCS levels for several days after DMBA administration. The levels are not sufficiently depleted to result in death of the animal although aphagia and diarrhea with resulting weight loss do occur. Administration of higher dosages of DMBA, 30.0 mg, results in death of the animals presumably due to adrenal apoplexy[2] and/or hypoadrenocorticalism. Our results lend support to part of the theory of WONG et al.[3], that there occurs a rapid depletion of adrenal steroid hormones following the administration of this potent carcinogen. We interpret the depletion of plasma CCS as a direct consequence of the cellular necrosis induced by DMBA. Whether, through this depletion of steroid hormones, a steric chemical inhibition is removed at the site of end organs influenced by adrenal cortical hormones, especially mammary tissue, is not known. If removal of these compounds allows DMBA or its metabolites to initiate the sequence of biochemical and biophysical events antecedent to tumor induction, it cannot be shown by our data. We observed plasma CCS fall following DMBA treatment and, in animals not sacrificed, subsequent mammary tumor formation but our data do not indicate a causal relationship between the two phenomena. The interaction of adrenal cortical hormones, other endocrine organs, their secretions and carcinogens is beyond the scope of our results[11].

Values[a] (µg%) for plasma levels of corticosterone following administration of DMBA

Time (h)	Control	DMBA
24	15.6	8.9
48	16.8	2.5
72	15.5	2.3
96	15.0	4.1
120	15.5	9.4

[a] Average for 15 animals from each group. Standard deviation of ± 1.4 for both groups of animals.

Zusammenfassung. Fluorometrische Messungen zeigten eine Abnahme von Plasmacorticosterone (CCS). Die Bedeutung dieser Resultate für theoretische Aspekte der Karzinogenese wird diskutiert.

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Heterozygote Zentrenfusion bei einer weissen Laborratte

Die zentrische Fusion akrozentrischer Chromosomen ist bei Rassen, Arten und höheren systematischen Einheiten als ein evolutionärer Vorgang bekannt, der Robertson-Prozess genannt wird (FORD und SHARMAN[1], CHU und BENDER[2], CHU und SWOMLEY[3], CORFMAN und RICHART[4], MATTHEY[5], ROBERTS[6] und HSU und ARRIGHI[7]). Aber auch intraindividuell ist ein Chromosomenpolymorphismus gefunden worden, der auf Zentrenfusion beruht (OHNO, STENIUS, FAISSIT und ZENZES[8] bei der Regenbogenforelle und BEÇAK, BEÇAK und OHNO[9] bei *Lepomis cyanellus*). Der gleiche Polymorphismus muss auch interindividuell – als primärer Mutationsschritt – auftreten. Diese Zentrenfusionen sind beim Menschen bekanntgeworden (LEJEUNE[10], CRAIG und LUZZATTI[11]) und beim Hausrind (HERSCHLER und FECHHEIMER[12], GUSTAVSSON[13]). Bekannt ist ferner ein Mäusestamm mit 2 metazentrischen Autosomen, die durch Zentrenfusion entstanden sind (LÉONARD und DEKNUDT[14]).

Hier soll nun über eine Zentrenfusion berichtet werden, die bei einer weiblichen weissen Laborratte beobachtet worden ist.

Das Tier (Nr. 5 in der Tabelle) stammte aus einer Wistar-Koloniezucht in Dänemark, deren Eltern vom Zentralinstitut für Versuchstierzucht in Hannover geliefert worden waren. Es war 2 Jahre alt, Verhalten und Gesundheitszustand entsprachen dem Alter. Das Tier war zufällig in einer kleinen Gruppe von einer grösseren Sen-

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