Plasmafeinstruktur besitzen. Insofern stimmen diese Befunde mit den Beobachtungen an anderen Neuroblasten von Hühnerembryonen überein[7,8]. Eine besondere und wahrscheinlich spezifische Eigenheit der Sympathicoblasten ist aber das Auftreten der dargestellten osmiophilen Grana. Über die chemische Natur dieser Grana können wir ohne histo- und biochemische Paralleluntersuchungen nichts Definitives sagen. Da es sich bei der Entwicklung der Sympathicoblasten um die Entwicklung adrenerger Neurone handelt, ist zu vermuten, dass die osmiophilen Grana Kondensationsprodukte von Katecholaminen oder Serotoninen sind. Aminreiche Nervenfasern besitzen ja recht typische osmiophile Grana von gleicher Struktur mit einem durchschnittlichen Kaliber von 600–800 Å. Über den Bildungsort dieser Grana während der Entwicklung vermögen wir noch nichts Sicheres zu sagen. Es ist anzunehmen, dass diese Grana bei der Entwicklung schon sehr früh im Perikaryon gebildet werden, um dann mit zunehmender Differenzierung über den axoplasmatischen Substanzstrom zu den Synapsen transportiert zu werden. Untersuchungen am fetalen sympathischen Ganglion des Menschen[9] haben keine vergleichbaren Grana offenbart; wir selbst haben identische Grana bei Sympathicoblasten von Entenembryonen gesehen.

Summary. With regard to the cytodifferentiation of neurones in the developing CNS and the spinal ganglia, only the sympathoblasts of the primary and secondary sympathic trunk of chick embryos contain a varying amount of catechol amine-containing granules. The formation of these granules takes place in rather early stages of development.

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Effects of Two Nephrotoxic Agents on New-Born Rats

It is known that the susceptibility of very young animals to toxic agents can differ from that of adults. In some instances a possible explanation is morphological and biochemical immaturity, as has been suggested in the case of the insusceptibility of the liver of new-born rats to several hepatotoxic agents[1]. At birth, the rat and mouse kidneys still contain some of the metanephros; histochemical[2,3] and electron microscopic[4] studies have demonstrated a progressive maturation of the tubular cells during the first weeks of life. The only study to our knowledge on the effects on new-born animals of compounds producing tubular necrosis in adults is a recent report of Wachstein and Robinson[5], who demonstrated that DL-serine and mercury are not effective in rats under 14 days of age. This finding has led us to investigate the effects on new-born rats of the synthetic amino acid S-dichlorovinyl-L-cysteine (DCVC), which in previous work with adult animals produced tubular necrosis in the kidneys and pancreatic damage as well as occasional periportal liver necrosis[6]. The LD_{50} of DCVC for adult male and female rats was respectively 66 (58–83) mg/kg and 83 (72–95) mg/kg[6].

The toxicity of DCVC for new-born rats is described in the present report. In addition, DL-serine has been tested under conditions comparable to those described by Wachstein and Robinson[5].

Wistar Porton rats, less than 24 h old, received in the dorsal area a subcutaneous injection of a freshly prepared 0.5% solution of DCVC in distilled water. Two litters with a total of 20 rats received 1 mg of DCVC per animal (approximately 200 mg/kg): on the following day, 16 were found dead and 4 had been cannibalized. The animals of each of 4 other litters were given either 0.5 or 0.25 mg of DCVC (respectively about 100 and 50 mg/kg): out of 20 rats given the higher dose only 3 survived more than 1 day and were killed for histology. Among 21 new-born rats receiving 0.25 mg of DCVC, 11 were kept under observation: of these 9 were alive after 3 days and 7 after 3 or 4 weeks, when they were killed. The other 10 animals were killed for histology in groups of 3 or 4 respectively 1, 2, or 3 days after the injection.

Paraffin sections were routinely stained with hematoxylin-eosin and with the PAS reaction. In all the animals observed within 3 days after treatment, microscopic renal damage was present, involving most of the formed tubules of the inner cortex which were markedly dilated and contained cellular debris with occasional pycnotic nuclei (Figures 1 and 2). On some occasions the epithelial layer was absent and the basal membrane faced the lumen. More frequently the epithelium was markedly thin and the brush border was poorly recognizable. From the 2nd day onwards necrotic, acidophilic, PAS-positive material was found in the lumen of several tubules, some of which were lined by normal epithelium. No damage was seen in the nephrogenic zone or in the medulla. Pancreatic damage was present in all the animals: among those receiving 100 mg/kg, necrosis and cellular disintegration were present; at the lower dosage the distribution of zymogen was quite irregular and the cytoplasm of many cells was uniformly and intensely acidophilic while the nucleus was displaced peripherically. Histological observations included also liver, spleen, thymus, sternal bone-marrow, and occasionally the adrenals: in none of these organs was there evidence of damage, except for one animal showing liver necrosis. Rats killed at the age of 3–4 weeks did not show pathological changes.

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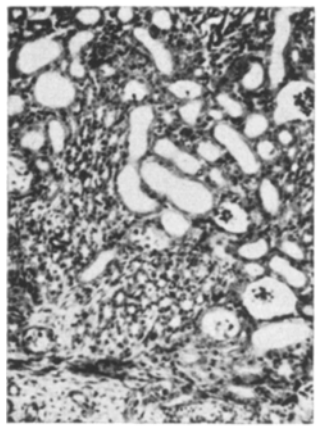

Fig. 1. Rat killed 24 h after the injection of 50 mg/kg DCVC. Renal inner cortex: tubules are dilated and lined by thin epithelium. Cellular and nuclear debris in the lumen. H. & E. × 70.

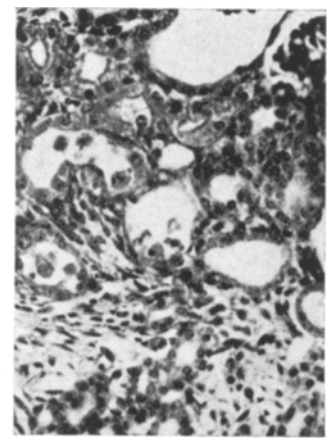

Fig. 2. Rat killed 24 h after the injection of 100 mg/kg DCVC. Borderline between inner cortex and medulla. Dilatation of cortical tubules showing no brush border and containing pycnotic cells. PAS × 130.

In another experiment, 16 new-born rats from 2 litters were injected with 5 mg of DL-serine (Merck, Darmstadt) as a 5% solution in distilled water (approximately 1000 mg/kg). They were killed in groups of 5 or 6 after 1, 2, or 3 days. As expected from the findings of WACHSTEIN and ROBINSON[5], none of these animals showed tubular changes. Also the other organs were normal. Two adult rats given the same dose per kg of DL-serine and killed 48 h later showed extensive tubular necrosis in the renal inner cortex.

The present experiments demonstrate that lethal and effective doses of DCVC are similar for new-born and mature rats and that tubular damage can be induced with this compound in the first day of life. It is obvious that the action of DCVC, the mechanism of which probably involves inhibition of mitochondrial enzymes related to respiration[7], is not modified in spite of the biochemical and morphological immaturity of the tubular cells in the new-born rat. This finding is comparable to the previous observation that dimethylnitrosamine, which does not produce tubular damage but evokes tumour formation in the kidneys, exerts this effect in new-born at least to the same extent as in adult rats[8].

In the case of DL-serine, a lack of nephrotoxicity in new-born rats was observed previously[5] and is confirmed in the present work. The difference between DL-serine and DCVC recalls the observation that the development of susceptibility to liver poisons corresponds to changes specific for each hepatotoxic agent[1]. However, whether the lack of nephrotoxicity of DL-serine in new-born rats is related to renal metabolism or to absorption, distribution and excretion remains to be ascertained[9].

Riassunto. Dei due composti DL-serina e S-diclorovinil-L-cisteina – che producono necrosi tubulare renale in ratti maturi – solo il secondo ha manifestato il medesimo effetto in ratti neonati. La differenza suggerisce che diversi gradi di maturità sono richiesti per consentire a ciascun composto di produrre danno tubulare.

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Über die farbgebende Gruppe von Crenilabrus-Blau[1]

Männliche Exemplare des Mittelmeerfisches *Crenilabrus pavo* C.V. besitzen besonders in der Brunstzeit eine auffallend bunte Färbung: Der Rumpf ist gelb mit roter Zeichnung; Kopf, Rücken und Flossen sind grünlichblau bis dunkelblau. Die blaue Farbe ist in der Hauptsache durch das Vorhandensein eines Farbstoffes (Crenilabrus-Blau) bedingt, doch dürfte auch die Struktur der Haut zur Intensität der Farbe beitragen. Während die gelben und roten Farbstoffe als Carotinoide (Astaxanthin- und Taraxanthinester) hinlänglich charakterisiert sind[2], ist die chemische Struktur der blauen Komponente bisher unbekannt.

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