adrenergic neurons (for review see e.g. Schildkraut and Kety[15,16]).

Zusammenfassung. 250 γ 6-Hydroxydopamin intraventrikulär pro Ratte vermindern nach 10 Tagen den Gehalt von Noradrenalin und Dopamin etwa um 50%. Hingegen wird 5-Hydroxytryptamin nur geringfügig beeinflusst. Das gleichzeitig gemessene exploratorische Verhalten und die lokomotorische Aktivität sind praktisch unverändert.

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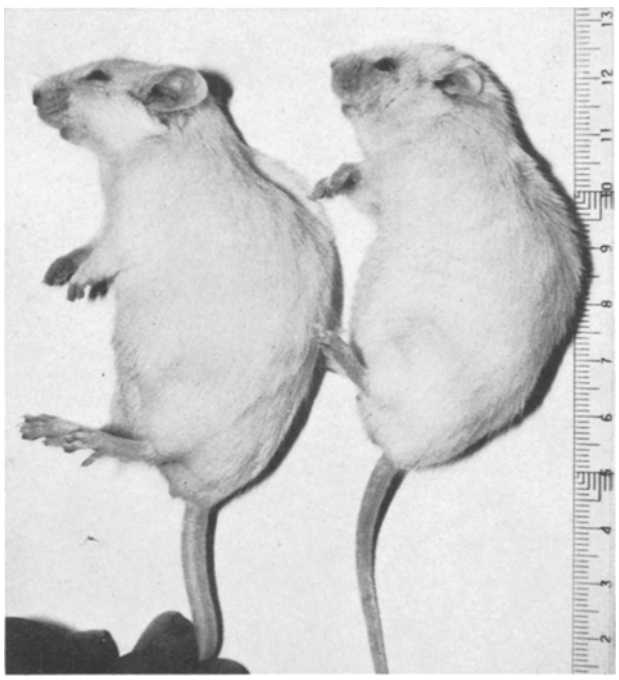
Malformations after Treatment of New-Born Mice with a Single Dose of Cyclophosphamide

The lethal and teratogenic effects of cytostatics and other drugs administered to fetus are the subject of much experimental study, while much less attention is paid to their effects when given to new-born animals. In investigations on the late effects of a single injection of cyclophosphamide in rats[1–3] and mice, we found that a single dose given to new-born mice resulted in malformations. As the drug is much used in human medicine a brief report may be indicated.

Swiss albino mice, less than 24 h of age and weighing 1–1.5 g, were given a s.c. injection of cyclophosphamide (Sendoxan, supplied by AB Pharmacia, Sweden), dissolved in distilled water, in doses ranging from 0.04–0.2 mg/mouse. In the experiments here described, all littermates were given the same treatment, as preliminary experiments had shown that water-treated controls grew much better than their cyclophosphamide-treated littermates and therefore might oust the latter from suckling.

At a dose of 0.2 mg/mouse or more there was a lethality of 100% (40 mice out of 40 died) within 7 days. At a dose of 0.08–0.1 mg/mouse, 18 out of 48 mice are alive after 6 months. All these mice are malformed, externally seen as a small stunted nose and short forelegs (Figure), but they show a normal behaviour. During the period of growth they are, however, much delayed, and grow more slowly and get hair much later than the controls. No detailed analysis has as yet been performed on the internal organs.



6-month-old mice. Right, treated with 0.08 mg cyclophosphamide at less than 24 h of age. Left, water-treated control. Note the stunted nose, short forelegs and ears of the treated mouse. Measurements shown in cm.

At a dose of 0.05 mg/mouse, 9 mice out of 10 are alive 6 months later, and at a dose of 0.04 mg/mouse none of 10 treated mice has died. In these 2 groups there are only a few showing malformations like the above-described.

A few of the treated females became pregnant. Those treated with a dose of 0.05 mg/mouse or less, apparently passed through their pregnancy and delivery without complications. Of females treated with a dose of 0.08–0.1 mg when new-born, however, 3 died during delivery, apparently because of a narrow pelvis. It should also be mentioned that of the surviving mice, treated with a dose of 0.08–1.0 mg, only 2 out of 18 are females. Apart from the 3 females mentioned, it has not been examined if those which died were pregnant.

As mentioned, treatment of new-born animals with cyclophosphamide does not seem to have been reported previously. The drug has, however, been much used in children in the treatment of malignancies, even down to an age of 9 days[4]. Cyclophosphamide is also used in children in non-malignant diseases as nephrosis[5]. To our knowledge no permanently adverse effects have been noted. Our observations may be a warning that during the period of growth such may appear, other than those intended on the hematopoetic and immunological systems[6].

Zusammenfassung. Cyclophosphamid in Einzeldosis an neugeborene Mäuse verabreicht, bewirkt Missbildungen von Kopf und Vorderextremitäten sowie Geburtshindernis.

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