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JOURNAL ARTICLE

Antimitotic drugs (cyclophosphamide and vinblastine) in the male rat. Deaths and behavioral abnormalities in the offspring

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The spermatogenesis and the offspring of male rats treated either with cyclophosphamide alone, or with both cyclophosphamide and vinblastine were investigated. The offspring were evaluated for the mean number of pups per litter, sex ratio, the frequency of apparent external malformations and, within the first 4 months of life, growth and mortality. When they reached adulthood and were between 12 and 16 weeks of age, the offspring were also examined for spontaneous activity and learning capacity. Treatment with cyclophosphamide or cyclophosphamide and vinblastine resulted in a decrease in the number of both primary spermatocytes and spermatids; the effect, however, lasted longer for the combined drug regimen. At birth, the animals sired by the treated males did not show any apparent malformations. However, compared with the control population the mortality rate of the offspring was significantly higher within the first 40 days of life; at adult age, the proportion of animals that failed in the learning ability test was significantly increased and those that did succeed showed impaired learning capacity. The difference, however, was significant only in the male offspring. Finally, the offspring's spontaneous activity was significantly decreased. No difference was found in mortality or behavior between the animals born of the cyclophosphamide or cyclophosphamide plus vinblastine-treated males. The behavioral disorders shown in the adult offspring confirm the existence of a long-term risk of paternal origin. This risk, essentially functional and independent of any morphologic pathology, should be taken into account in the context of environmental genotoxicity.