Damage to Spermatogenesis in Juvenile Rat Treated with DDVP and Malathion

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An advantage of organophosphate insecticides which include dichlorvos (DDVP) and malathion, is that they undergo fast degradation in the environment. Consequently they are safer than older chlorinated hydrocarbon insecticides like DDT as regards cumulation in the environment.

However, their acute toxicity is generally higher, the levels for DDVP and malathion being given as 60 - 80 mg/kg for i.v. administration and up to 400 mg/kg for oral administration (PERKOW 1971).

Interference with fertility is an aspect seldom discussed to date. Our research group noted that damage was caused to the testes of male mice following administration of DDVP (KRAUSE and HOMOLA 1974). Assuming that maturing organs would be damaged more severely than fully mature ones, we therefore evaluated this compound for its effect on spermatogenesis in juvenile rats.

Materials and Methods

Eighty juvenile male Wistar rats were divided into groups of 16 each. The groups received the following treatments:

Group 1: 0.1 ml of olive oil daily from the 4th to the 23rd day of life.

Group 2: 20 mg DDVP/kg on the 4th and 5th day of life.

Group 3: 10 mg DDVP/kg daily from the 4th to the 23rd day of life.

Group 4: 40 mg malathion/kg on the 4th and 5th day of life.

Group 5: 20 mg malathion/kg daily from the 4th to the 23rd day of life.

On the 6th, 12th, 18th, 26th, 34th, and 50th day of life, 2 rats of each group were sacrificed and their testes were histologically examined by the recently described method (KRAUSE *et al.* 1975).

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Results

Body weights, weights of testes and the ratio of tubulus to interstitial tissue showed no significant alterations attributable to the treatment. Quantitative evaluation of the tubular cells showed alterations particularly in the period of administration, these being greatest following application of malathion at a dose of 40 mg/kg.

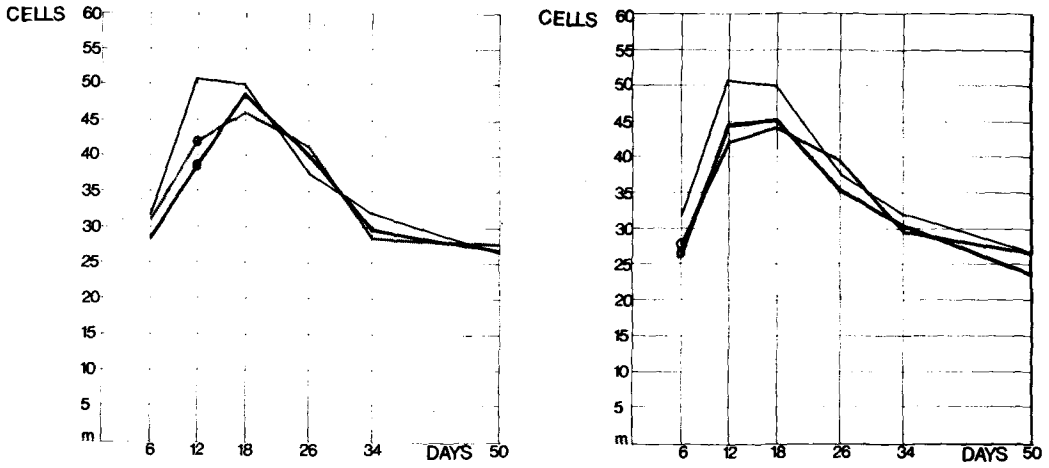

Fig. 1. Number of Sertoli cells per tubulus cross section after DDVP (left) and Malathion (right) ——— control; ▬▬ group 2 resp.4; - - - -group 3 resp.5. Significant differences are marked by a(o). The Sertoli cells were significantl reduced on the 6th day.

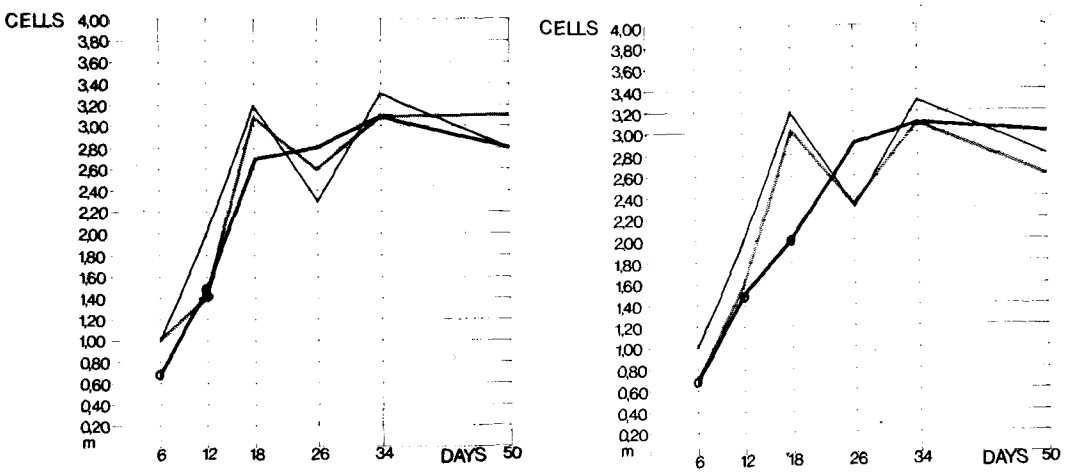

Fig.2. Number of A-spermatogonia per tubulus cross section after DDVP (left) or Malathion (right). Legend see fig.1. The A-spermatogonia were reduced on the 6th and 12th day by malathion and DDVP.

Discussion

The damage caused to spermatogenetic tissue by DDVP and malathion is of a relatively slight nature and is confined to the period of administration. The worst damage is seen following 2 applications of malathion each at 40 mg/kg.

It is noticeable that pachytene spermatocytes and Leydig cells are also damaged in addition to sertoli cells and A-Spermatogonia. This is indicative of damage commonly affecting all cell groups.

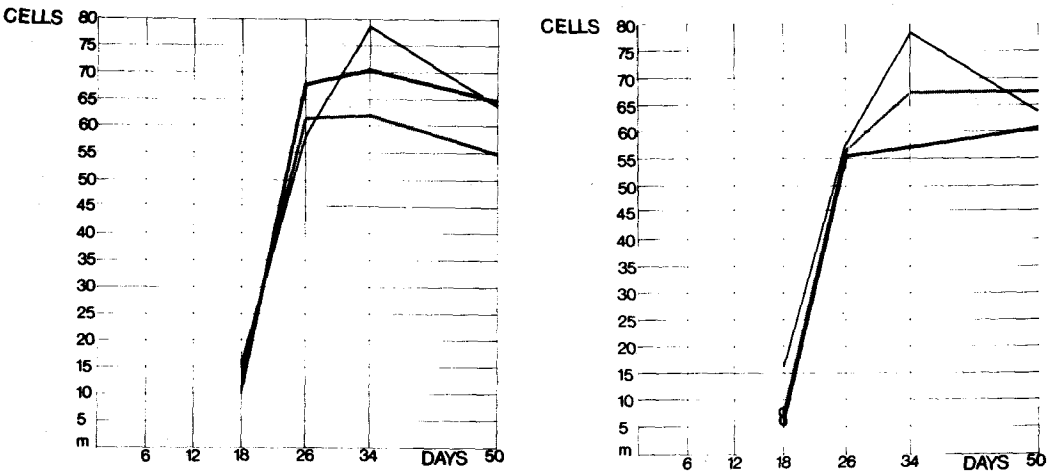

Fig. 3. Number of pachytene spermatocytes per tubulus cross section after DDVP (left) or malathion (right). Legend see fig. 1. Reduction in pachytene spermatocytes was significant only on the 18th day.

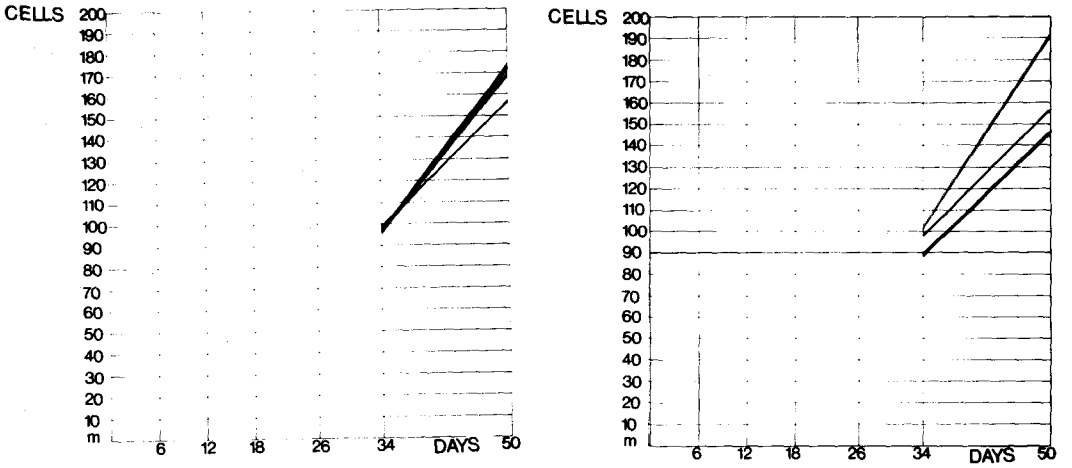

Fig. 4. Number of spermatids per tubulus cross section after DDVP(left) or malathion (right). Legend see fig.1. No significant reduction was noted for the spermatids. All alterations returned to normal by the 50th. day.

It has been reported that DDVP has a cytostatica-like, mitosisinhibiting effect (HILGETAG and TEICHMANN 1965) and chromosome breaks were also seen (LÖFROTH 1970). However, this effect need not involve only the mitoses of the A-Spermatogonia as in the case of cyclophosphamide (HILSCER and REICHELT 1967), but also the mitoses of the B-Spermatogonia, the final mitosis before meiosis (LEBLOND and CLERMONT 1952).

The simultaneous reduction of the number of Leydig cells (which can be other than just relative to the tubulus cross-section because the ratio of tubulus to interstitial tissue remains unchanged) need not be accounted for solely by inhibition of mitosis. When Leydig cells lose their metabolic activity, they can no longer be clearly distinguished from fibrocytes of the interstitial tissue.

As organophosphates have a general esterase depressing effect, it is most conceivable that as a result of this influence on metabolism the Leydig cells undergo regression (HAUSCHILD 1965).

This would also suggest a reduction of androgen biosynthesis. Androgens, however, especially testosterone, are absolutely essential to quantitatively normal development of spermatogenesis (STEINBERGER 1971). Therefore, the transient interference with spermatogenesis seen after administration of DDVP and malathion may also be accounted for by a testosterone reduction. The same was assumed for DDT although by a different mechanism (KRAUSE et al. 1975).

The disturbances return to normal by the 50th day of life. As the tested compounds do not cumulate and are not stored, they

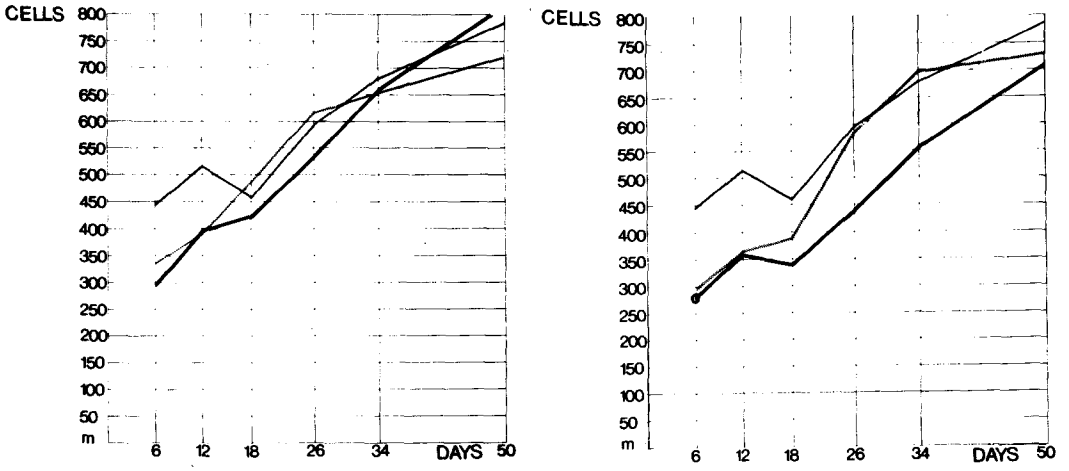

Fig. 5. Number of Leydig cells per mm^2 of testis section after DDVP(left) or malathion (right). Legend see fig. 1. A significant reduction in Leydig cells was seen on the 6th day in the group which received malathion at a dose of 40mg/kg. In the reproduction study, the litters produced by the treated animals did not differ from those of the controls.

do not continue to have a direct effect after the end of the application.

Summary

Juvenile male rats received either 20 mg DDVP or 40 mg malathion/kg on the 4th and 5th day of life, and either 10 mg DDVP or 20 mg/kg malathion daily from the 4th to the 23rd day of life. The histological examination of the testes showed slight reductions of the spermatogenetic cells and Leydig cells. Therefore, it is assumed that testosterone synthesis is reduced, followed by damage to spermatogenetic cells. All disturbances return to normal by the 50th day of life.

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