and noradrenaline remain normal, noradrenaline forming about 16 per cent of the total amine, and there is no evidence of a selective loss of either amine such as occurs in association with insulin hypoglycæmia. Insufficient pressor amine was extracted from glands after injections of 5 mgm./kgm. and more to allow an estimate of the individual amines.

It should be noted that glands removed 24 hr. after an injection of reserpine show an increase in weight as compared with controls. This change is due to cortical hypertrophy and is associated with an increase in the esterase content of the inner part of the zona fasciculata and the zona reticularis. As a result of this change, the adrenals show an abnormally low content of pressor amines if these are given as per gm. of adrenal weight, and it is therefore preferable to give the catechol amine content per rat (providing rats of uniform age and weight are used), or per unit body-weight.

I would like to express my thanks to Ciba Laboratories, Ltd., for supplies of reserpine ('Serpasil').

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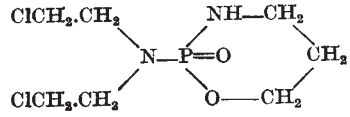
Chemotherapeutic Action of a Cyclic Nitrogen Mustard Phosphamide Ester (B 518-ASTA) in Experimental Tumours of the Rat

THE synthesis of new cytostatic drugs is governed by the attempt to find new substances which unite maximum therapeutic effectiveness with minimum toxicity. For this purpose it seems to be advantageous not to apply the substance in its active form, but by introducing suitable chemical groups to transform it into an inert transport substance which will be reconverted into the active form at the site of therapeutic action in the body. This principle has already proved of value in the treatment of prostatic carcinoma with stilbœstrol diphosphate[1].

Using the same method, Friedman and Seligman[2] combined the active *bis*-(β-chlorethyl)amino-group with phosphoric acid. The resulting compounds proved, however, to be therapeutically ineffective. In our experiments we allowed *bis*-β-chlorethyl-phosphamide-dichloride to react with alkanolamines. Thus we obtained cyclic *bis*-(β-chlorethyl)-phosphamide esters with two phosphamide bonds and one ester bond. Chemical analysis has shown that the basicity of the phosphamide nitrogen and thus also the reactivity of the chlorine atoms are considerably reduced. In comparison with *bis*-(β-chlorethyl)amine (nitrogen mustard, HN2), the rate of chlorine ion liberation in aqueous solution (at 37° C.) is considerably lowered.

The examination of the therapeutic effectiveness of numerous homologous compounds in different graft tumours of the rat has shown B 518-ASTA to be particularly effective and well tolerated. B 518 is the experimental designation of the cyclic propanol-amido-ester of *bis*-(β-chlorethyl)-phosphamide. Its trade name is 'Endoxan R', Asta-Werke A.G., Brackwede (Germany).



The minimum lethal dose of B 518 in the rat is 160 mgm./kgm., whereas for N-oxide mustard the minimum lethal dose is only 50 mgm./kgm., and for nitrogen mustard even as low as 1·5 mgm./kgm. Thus the toxicity of B 518 is remarkably low.

In therapeutic trials on fully developed tumours of the rat, for example, the solid Yoshida sarcoma (20 gm.), Walker-256-carcinoma (1 gm.) and Jensen sarcoma (5 gm.) we obtained a definite cure with a single intravenous injection of B 518. The medium effective dose (*DC*50) was found to be 3·9 mgm./kgm. for the Yoshida sarcoma, 6·0 mgm./kgm. for the Walker carcinoma and 3·6 mgm./kgm. for the Jensen sarcoma, that is, it amounts to only 2–4 per cent of the minimum lethal dose. Thus the therapeutic index of B 518 is more than twice as wide as that of N-oxide mustard and about 10 times as large as that of the ethylenimines such as TEM, TSPA and *E* 39-BAYER. In addition, B 518 proved to be the only substance which considerably inhibited the DS-carcino-sarcoma previously resistant to all other compounds[3].

In vitro tests, in which B 518 was incubated with tumour cells at 37° C., showed complete inertness of the compound up to a concentration of 10^{-3} gm./ml., the cells being then grafted on to healthy young rats and their taking capacity checked. This makes it appear probable that the cyclic propanol amide ester of *bis*-(β-chlorethyl)-phosphamide actually represents an inert transport form, from which the highly active form is liberated only within the body.

The results will be published more fully in further papers[4].

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'Compensatory Hyper-regeneration' in the Antennæ of Hemiptera

WOLSKY[1] claims that prior to his 1957 demonstration, under the above title, there was no experimental evidence to show that the antennal oligomery frequently encountered in Hemiptera Heteroptera results from the unusual course regeneration takes after larval injury. But in 1829 Heineken[2] amputated the antenna of a reduviid larva and obtained an adult exhibiting just those features which Wolsky now notes. Gäbler[3] studied antennal regeneration in three families of Heteroptera, and Balazuc[4], unaware of Gäbler's work, has given a full account of regeneration in a reduviid. In addition, the literature abounds with references to the field occurrence of