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George M. Martin

Department of Pathology,
University of Washington School of Medicine,
Seattle 5, Washington.

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IMMUNOLOGY

Inhibition of Immune Processes by 'Melphalan'

The cells responsible for the immune response vary in susceptibility to inhibitory agents at different stages of the response. Radiation and busulphan ('Myleran') inhibit the response to the greatest degree if administered before the antigen and are relatively ineffective if given afterwards[1,2]. Alkylating agents other than busulphan (the mustards and ethylene imines) and the antimetabolites are most effective if given some 1–3 days after the antigen and are less effective if given beforehand[2,3].

It might therefore be expected that the survival of homografts would be prolonged to the greatest extent by administration of alkylating agents (other than busulphan) or antimetabolites after grafting and little affected by their administration before grafting. This has been found to be the case for amethopterin in mice and guinea pigs[4] and *cyclo*phosphamide in mice[5].

Glynn, Bianco and Goldin[4], however, found that, whereas pretreatment of recipients with amethopterin (5 mg/kg daily for 5 days before grafting) failed to prolong survival of homografts of *DBA*/2 skin or tumour to *BALB*/*c* mice, pretreatment with 'Melphalan' (L-*p*-(di-2-chloroethylamino) phenylalanine) in this dosage was effective. Since 'Melphalan' is a mustard, with *in vitro* and *in vivo* effects similar in many ways to those of other mustards[6], this finding is unexpected. It suggests that 'Melphalan', unlike other mustards so far examined, might inhibit immune processes if given before the antigen. The following experiment was therefore performed.

Male *A2G* mice, weighing 15–24 g, were injected intravenously with 0·1 ml. of a 10 per cent suspension of sheep red cells in physiological saline. 'Melphalan' or amethopterin, ground in saline immediately before injection, was given in single doses of 15 mg/kg subcutaneously at various times before or after the antigen. The mice were bled seven days after the antigen injection, and their sera titrated individually for hæmagglutinins. Doubling dilutions of serum in saline were made in WHO hæmagglutination trays and mixed with equal volumes (0·4 ml.) of a 1 per cent suspension of sheep red cells in saline. The trays were incubated at 37° C for 0·75 h and agglutination patterns read after they had stood for a further 1–2 h at room temperature[7].

Results are shown in Fig. 1. The titre in control mice was $1/2^{6\cdot8} \pm 1\cdot1$. It is clear that although 'Melphalan' resembles most other alkylating agents in its ability to suppress antibody production when given after the antigen, it is also able to suppress the response effectively if given up to 3–4 days beforehand. Smaller doses (5 or 10 mg/kg) inhibited antibody production when given up to 2 days before the injection of antigen. These findings explain the apparently anomalous behaviour of this mustard in inhibiting the homograft response when given before grafting. Amethopterin, on the other hand, had, as expected, little effect on antibody production when it was given before the antigen and was maximally inhibitory when given some 1–2 days afterwards.

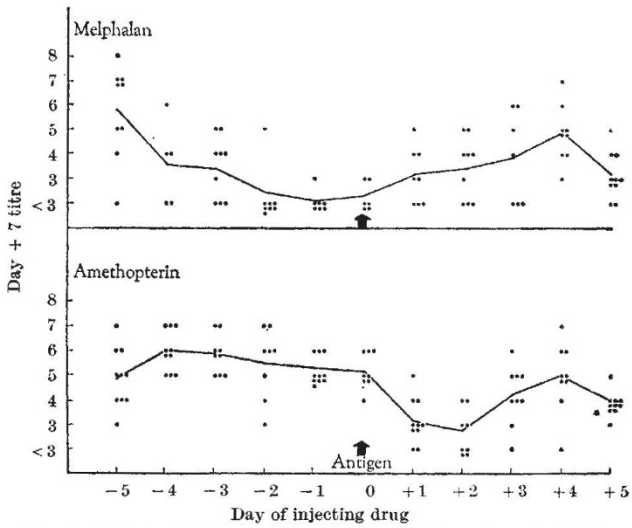

Fig. 1. Effects of 'Melphalan' and amethopterin on hæmagglutinin production. Mice injected with sheep red cells on day 0 and with 'Melphalan' or amethopterin, 15 mg/kg, before or after injection of antigen. Sera taken on day + 7 and titrated individually. Titres are shown as reciprocals of the end-point dilutions, expressed as powers of the base 2. Titre of controls was 6·8 ± 1·1

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I. N. Brown

Glaxo Research, Ltd.,
Greenford, Middlesex.

M. C. Berenbaum

Surgical Unit,
St. Mary's Hospital Medical School,
London, W.2.

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RADIOBIOLOGY

Influence of Gamma-irradiation on Sulphur-35 Mineralization of Sternum and Tibia, and Weight of Spleen and Testes of Chicks

The radiation syndrome of chicks exposed to X-rays[1,2] included renal damage, kidney hæmorrhages, ulceration of œsophagus, gastrointestinal mucosa destruction, anæmia, liver hæmorrhages and mortality. Young chickens were reported to be more sensitive to radiation than older ones.

The cysteine-cysteamine group[3] represent the most effective class of sulphur compounds which give some protection against irradiation. Cysteine was found to be an effective compound in radiation protection[4]. Gluta-