putation of Melbourne University. This study was supported by the National Health and Medical Research Council, Canberra, Australia; the US Public Health Service; the US Atomic Energy Commission; and the International Atomic Energy Agency. J. J. M. is a postdoctoral fellow of the American Cancer Society. V. X. G. is a Roche fellow.

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Received September 3, 1968.

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Immune Paralysis of Thymus Cells by Bovine Serum Albumin

IT has been observed consistently that the immune responsiveness of neonatally thymectomized mice to various antigens, including bovine serum albumin (BSA), can be restored by injection of sufficient dissociated thymus cells[1,2]. This is also true for mice thymectomized in adult life, lethally irradiated and injected with bone marrow (my unpublished data). Claman, Chaperon and Triplett[3] have shown that the transfer of thymus cells alone to irradiated recipient mice would not restore their antibody response to sheep erythrocyte antigens, but that these cells would act in cooperation with bone marrow cells when a mixture of these cell types was transferred.

It has been reported recently that thymus cells play a specific part in the antibody response to sheep erythrocytes[4], and that treatment of thymus-grafted mice with large doses of sheep erythrocytes would depress the proliferative response of the thymus-derived cells to a further dose of this antigen[5].

Experiments were therefore initially set up to demonstrate thymus–marrow cooperation when BSA was used as antigen, and then an investigation was made on which of these two cell types would carry the specific alteration involved in immune paralysis. The recipient mice were irradiated with 900 r., and injected on the same day first with mixtures of thymus and marrow cells from syngeneic donors and then with an immunizing stimulus consisting of alum-precipitated BSA mixed with 2×10^9 killed *Bordetella pertussis* organisms (personal communication from D. Dresser). The animals were bled 21 and 35 days later and the serum antibody was titrated as antigen binding capacity (ABC) by a modification of Farr's ammonium sulphate method[6]. It was found that for a constant dose of thymus cells the response declined with declining doses of marrow cells, and with a constant dose of marrow cells the response declined with declining doses of thymus cells. This provided the criterion for cooperation.

In a second experiment the donors were injected with 10 mg of BSA (Cohn fraction V) in saline, one day before cell transfer. When thymus from BSA-treated donors was transferred together with normal marrow cells the response was profoundly depressed (ABC = 0·1 μg/ml.); but when marrow cells from BSA-pretreated donors were combined with normal thymus cells scarcely any inhibitory effect was observed which could have been attributed to pretreatment with BSA (ABC = 4·0 μg/ml.).

As a measure of the quantity of BSA which penetrated to the donor cells and was transferred with them to the recipients, an injection was made of ^{131}I-labelled BSA to normal mice. These were killed one day later and radioactive counts were made on the washed thymus and marrow cells. From this it was clear that not more than 0·05 μg of BSA could have been transferred to each recipient, and it was also apparent that about twice as much antigen was transferred with marrow as with thymus cells. To demonstrate that the effect of pretreating the thymus donors was not due merely to the antigen they carried, a third experiment was performed. Recipient mice were injected with normal marrow and thymus cells, together with pretreated cells of either thymus or marrow origin. In neither case did the pretreated cells abolish the response of the normal cells, although a marginal effect was observed with pretreated thymus cells.

It is concluded that thymus cells and marrow cells can cooperate in the immune response to BSA; and that pretreatment of the donors with BSA one day before cell transfer can make their thymus cells but not their marrow cells unresponsive to BSA. It remains to examine the specificity of this unresponsive condition before concluding that thymus cells can carry immune paralysis towards BSA.

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Received August 6, 1968.

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Effects of Antilymphocyte Serum on Induction of Tumours and Leukaemia by Murine Sarcoma Virus

THE suppression of immune reactions has helped to analyse their role in controlling neoplastic growths. The frequency of neoplasms which contain virus-specific transplantation antigens usually is strikingly increased in animals thymectomized during the neonatal period or given antilymphocyte serum (ALS). Experimental animals infected with *SV* 40 virus, adenovirus type 12, and polyoma virus—oncogenic viruses that do not induce tolerance—or with the murine sarcoma virus (MSV) show more tumours at an earlier age if they are thymectomized or treated with ALS (refs. 1–6). In at least one system using induction by polyoma virus of neoplasms in C57Bl mice, the major determinants of tumour induction and control have been shown to be the virus-specific transplantation antigen and the immune response of the tumour bearing host[7].

Antiserum against lymphoid cells (ALS) has been shown to be an effective suppressant of cell-mediated immune responses such as skin graft rejection and delayed hypersensitivity reactions[8–10]. Those processes which lead to the production of humoral antibody are also sensitive to ALS (ref. 11), but may have unusual time-dependent relationships to antigen administration[12]. It was inter-