References and Notes

1. C. O. Miller, *Ann. Rev. Plant Physiol.* **12**, 395 (1961).
2. P. L. Goldacre and W. Bottomley, *Nature* **184**, 555 (1959).
3. C. O. Miller, F. Skoog, F. S. Okumura, M. H. Von Saltza, F. M. Strong, *J. Am. Chem. Soc.* **78**, 1375 (1956).

4. Thanks are due G. Messer for technical assistance. This is contribution No. 524-E, 1962 series, from the National and University Institute of Agriculture, Rohovot, Israel.

9 August 1963

Thymus: Its Limited Role in the Recovery of Homograft Response in Irradiated Mice

Abstract. *Adult mice subjected to thymectomy or sham thymectomy received lethal irradiation and subsequent protective infusion of syngeneic bone marrow. Thirty days later they received allogeneic and xenogeneic skin grafts. Donors of the xenogeneic grafts were rats. The thymectomized mice rejected the grafts of rat skin only slightly later than the controls did; in contrast, the time of retention of allogeneic grafts was significantly longer in the thymectomized mice.*

Recent reports (*1*, *2*) have indicated that the thymus in an adult animal is essential for the complete recovery of the homograft response after irradiation at lethal and sublethal dosages. However, work at the U.S. Naval Radiological Defense Laboratory, San Francisco (*3*), suggests that, while a normal homograft response toward allogeneic grafts appears to be dependent upon normal thymic function, the thymus of the adult mouse plays little or no role in the rejection of xenogeneic skin grafts from rat donors. The work of Miller *et al.* (*2*) with thymectomized adult mice that had received irradiation at lethal dosages and protection against the lethal effects of the radiation through subsequent infusion of syngeneic bone marrow provided an excellent experimental model with which to further evaluate the role of the thymus in the rejection of allogeneic and xenogeneic skin grafts.

In male mice 12 to 14 weeks old, of strain (C57L × A)F_1 (hereafter designated "LAF_1") thymectomies or "sham thymectomies" were performed according to the method of Miller (*4*). One week after surgery the mice received 870 rad of whole-body x-radiation [LD_{99} + 100 rad: 250 kv(peak), 15 ma; half-value layer, 1.5 mm Cu; 30 rad/min]. Immediately after irradiation the mice received an intravenous infusion of syngeneic bone marrow cells (3.0×10^6 cells). Thirty days after irradiation the surviving mice received grafts of syngeneic, allogeneic, and xenogeneic skin. Donors of the allogeneic grafts were mice of a strain that differed from that of the recipient with respect to the H2 locus. The donors of the skin grafts were adult male mice of strains $LAF_1(H2^{ab})$, BALB/c ($H2^d$), and (C3H × DBA/2)F_1 (or "C3D/2F_1") ($H2^{kd}$), and 3-week-old male Sprague-Dawley rats. The method of Bailey and Usama for orthotopic grafting of tail skin was used (*5*). Details of the grafting and the criteria of rejection (total destruction of the engrafted tissue) have been reported elsewhere (*3*). In Table 1, mean survival time of the grafts, with standard deviation, is reported for the groups in which the rejection of all grafts was complete at the time of writing. The survival time for each graft is reported for the groups in which some allogeneic grafts remained intact.

Eight of nine mice (strain LAF_1) in which sham thymectomies had been performed and 10 of 12 thymectomized mice of the same strain survived irradiation. The mice subjected to sham thymectomy rejected allogeneic grafts in approximately 14 days and grafts of rat skin in 10 days (Table 1). The thymectomized mice rejected rat grafts in approximately 14 days; in contrast, the first allogeneic graft was rejected at 18 days after grafting, and 11 of 20 grafts were intact 40 days after grafting.

These experiments suggest that the recovery of at least one function of the "immune mechanism"—the function of the rejection of xenogeneic grafts—after irradiation of lethal dosages is not dependent upon the presence of the adult thymus. These and other data (*3*, *6*) suggest, further, that grafts of xenogeneic solid tissue are rejected by a cell system functionally and physiologically distinct from the "thymus-dependent mechanism" (*2*).

Failure of syngeneic bone marrow with its lymphoid cell component (*7*) to restore the normal "lymphopoietic and immune functions"—the function of the rejection of allogeneic grafts—in these mice underlines the importance of the host contribution to the immune mechanism of the radiation chimera. It appears that the host contributes its thymic regulatory apparatus (*1*, *2*, *8*) and perhaps the cell system which deals with grafts of xenogeneic solid tissue (*9*).

Table 1. Rejection of allogeneic and xenogeneic skin grafts by adult mice of strain LAF_1 that had been subjected to thymectomy, or sham thymectomy, and irradiation at lethal dosages. The mice were protected against the lethal effects of the x-irradiation by an infusion of cells of syngeneic bone marrow.

No. of mice	Survival time of graft (days)*		
	Strain BALB/c	Strain C3D/2F_1	Rat
	Sham thymectomy		
8	14.1 ± 4.2†	14.7 ± 3.0†	10.0 ± 1.4†
	Thymectomy		
10	18, 25, 30, 30, 35, 40, 40, 40, 40, 40, respectively	28, 30, 32, 32, 40, 40, 40, 40, 40, 40, respectively	14.0 ± 2.4†

* Times as of day 40 after grafting. † Means, plus or minus standard deviation.

MARVIN L. TYAN
LEONARD J. COLE
WILLIAM E. DAVIS, JR.
Biological and Medical Sciences Division, U.S. Naval Radiological Defense Laboratory, San Francisco 24, California

References and Notes

1. J. F. A. P. Miller, *Nature* **195**, 1318 (1962).
2. ———, S. M. A. Doak, A. M. Cross, *Proc. Soc. Exptl. Biol. Med.* **112**, 785 (1963).
3. M. L. Tyan and L. J. Cole, *Transplantation* **1**, 365 (1963); *J. Immunol.*, in pre→ *Science* **141**, 813 (1963).
4. J. F. A. P. Miller, *Brit. J. Cancer* **14**, 93 (1960).
5. D. W. Bailey and B. Usama, *Transpl. Bull.* **7**, 424 (1960).
6. M. L. Tyan and L. J. Cole, *Transplantation*, in press.
7. C. E. Ford, J. L. Hamerton, D. W. H. Barnes, J. F. Loutit, *Nature* **177**, 452 (1956); N. Gengozian, I. S. Urso, C. C. Congdon, A. D. Conger, T. Makinodan, *Proc. Soc. Exptl. Biol. Med.* **96**, 714 (1957); J. F. Loutit, in *Ciba Foundation Symposium on Transplantation*, G. E. W. Wolstenholme and M. P. Cameron, Eds. (Churchill, London, 1962), p. 399.
8. W. E. Davis, M. L. Tyan, L. J. Cole, *Transplantation*, in press.

9. The studies reported here were supported in part by funds from the Bureau of Medicine and Surgery, U.S. Navy.

19 August 1963