flattened between its surface and the underside of the cover slip. This caused some of the protoplasts to assume an appearance similar to erythrocytes, with a dark outer edge and a light central area. It was in this central area that flickering was most readily visible.

The above technique is also useful for obtaining photographs of a large number of live organisms (particularly highly motile ones) at one time, since intact cells are not flattened by this procedure.

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Thymus: Its Role in Lymphoid Recovery after Irradiation

Abstract. *Regeneration of spleen lymphoid centers after destruction of lymphoid tissues is dependent on the thymus.*

As a result of experiments with embryonic (*1*) and neonatal (*2*) thymus, a resurgence of interest has developed in the idea that the thymus represents the major primordium of the mammalian lymphoid immunological system (*3*). Experiments directed toward understanding the mechanics of thymus lymphopoesis have shown that the thymus is an autonomous lymphoid organ capable of morphogenesis in vitro as well as upon transplantation (*1*, *4*). Removal of the thymus from neonatal animals leads to depletion of lymphoid cells from various lymphoid organs as well as from the circulation (*2*).

That the thymus can play a role in adult life as well as in the embryonic and neonatal period has already been clearly demonstrated in studies of murine leukemias (*5*). A role for the thymus in normal lymphoid function has also been proposed (*6*, *7*), but the nature of this role has not been well defined. The possibility that the thymus in the adult mouse influences lymphopoeisis in a manner analogous to that seen during development was examined in the experiments reported here.

To determine optimal experimental conditions, a series of experiments were performed to establish the radiation sensitivity of thymus lymphoid differentiation. Thirty thymus rudiments were removed from 12-day-old mouse embryos. They were irradiated with 140 kv (peak), 5 ma x-rays with ½ mm Al filtration at a dose rate (in air) of 80 r/min. Doses ranged from 600 to 1500 r. The thymuses were then grown for 1 week in vitro under conditions known to promote differentiation of thymus lymphoid cells (*4*). Doses up to 900 r failed to interfere appreciably with subsequent lymphoid morphogenesis. In a series of exploratory runs 900 r was effective in destroying the lymphoid cells of the adult spleen. This dose was therefore chosen to assess the function of the adult thymus. Ten F_1(C3HxAKR) male mice were thymectomized at 3 to 4 weeks of age and irradiated with 900 r x-rays at 10 weeks of age. Ten nonthymectomized, irradiated litter-mates served as controls. Ten days after irradiation the animals were killed, and the spleens were prepared for histological examination. In nine out of ten control mice, early signs of recovery were seen in the accumulation of lymphoid cells in spleen lymphoid centers. In all ten thymectomized, irradiated mice, on the other hand, such lymphoid cell accumulations were lacking.

These experiments are particularly pertinent with regard to Miller's finding that recovery of immunological function after irradiation is impaired by thymectomy of adult animals (*8*); our results suggest the cellular basis for his observations. Neither in Miller's experiments nor in ours has it been determined whether the role of the thymus is indirect—that is, through production of a lymphocytosis stimulating factor (*7*) or by providing a tissue environment conducive to differentiation of nonthymic cells (*8*)—or, on the other hand, direct, by contribution of cells which migrate to the spleen (*3*). Indeed, the alternatives are not mutually exclusive, for a few generative cells, migrating from the thymus to the spleen, might well serve as centers for induced differentiation of lymphoid cells. Experiments involving marked cells, extracts, and transplants are necessary before merits of various alternatives can be assessed critically (*9*).

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Antigenicity of Polypeptides: Immunological Unresponsiveness to Copolymers of α-Amino Acids

Abstract. *Immunological tolerance toward three synthetic random copolymers of the α-amino acids, glutamic, lysine, alanine, and tyrosine, was produced by a single injection of the polymers into newborn rabbits. The tolerant state could be extended by an additional intravenous injection of antigen. Repeated injections of the polymer in adjuvant mixture could "break" the tolerant state.*

The antigenicity of random copolymers of L-α-amino acids has been investigated in rabbits (*1–3*), guinea pigs (*4*, *5*), and man (*6*), with an aim of learning about the chemical basis for immunogenicity. Studies of the multichain polypeptide antigens (*2*) have also contributed to the existing knowledge on the molecular requirements for antigenicity. This study was undertaken to determine whether random copolymers could induce a state of immunological unresponsiveness in rabbits similar to that induced by other nonliving antigens, mainly serum proteins (*7*).

The percentage composition in moles of the amino acids in the random copolymers used in this study is indicated by the subscript. The polymers glu_{60} ala_{40} (GA); glu_{42} lys_{28} ala_{30} (GLA30),

Table 1. Production of unresponsiveness in rabbits by injection of copolymers of alpha amino acids within 24 hours after birth. The results are based on passive cutaneous anaphylactic tests (adj., adjuvant; i.v. intravenous injection).

Group	Injections given	Rabbits reacting after immunizations	
		1st*	2nd†
	GA		
I Test	adj., adj.	0/12	7/11
I Control	adj., adj.	5/7	4/7
II Test	i.v., adj.	0/6	0/6
II Control	i.v., adj.	0/3	3/3
	GLA30		
I Test	adj., adj.	0/12	9/12
I Control	adj., adj.	5/6	5/6
II Test	i.v., adj.	0/6	0/6
II Control	i.v., adj.	1/4	2/4
	GLAT		
I Test	adj., adj.	0/9	8/8
I Control	adj., adj.	5/5	5/5
II Test	i.v., adj.	2/10	5/10
II Control	i.v., adj.	4/5	5/5

* Results obtained 3rd week after adjuvant or last intravenous injection. † Results obtained 3rd week after second adjuvant injection.

and glu_{36} lys_{24} ala_{35} tyr_5 (GLAT) have been described previously (*3*, *4*, *6*). The average molecular weights were 33,000, 62,000, and 35,000, respectively.

Unresponsiveness was induced by injecting New Zealand white rabbits intraperitoneally within 24 hours after birth with 100 mg of the antigen. Eighteen animals were used for each antigen and litter mates were kept as controls (ten rabbits per antigen). At 2½ months of age, the experimental and control rabbits were bled for serum and then divided into two groups. Animals of group I were injected in the toe pads with 20 mg of the polymer in complete Freund's adjuvant. The animals were bled after 2 and 3 weeks. Three weeks later, the animals received another injection of the polymer in adjuvant and were bled again after 2 and 3 weeks.

The rabbits in Group II received an intravenous injection of 20 mg of the polymer in solution on day 1 (2½ months of age), day 8 and day 22; they were bled 1 week and 3 weeks later. The rabbits were then injected with 20 mg of the polymer in complete adjuvant. Serums were obtained 2 and 3 weeks later. All serums were tested for the presence of antibody by the passive cutaneous anaphylaxis method (*8*), and the serums from animals injected with GLA30 and GLAT were tested by the passive hemagglutination method (*3*). This latter method could detect both 7*S* and 19*S* antibody. All serums that were negative by the passive cutaneous anaphylaxis test were also negative by the hemagglutination test.

To test the specificity of the depressing effect of the injections of polymer which had been given soon after birth, all rabbits were also injected with bovine serum albumin. Normal responses were noted in all animals.

The results presented in Table 1 indicate that although immunological tolerance was produced in a large proportion of the rabbits injected with each of the antigens on the day of birth, the tolerant state was limited. Of the rabbits in Group I that received adjuvant injections of the polymer 6 weeks apart, seven out of eleven, nine out of twelve, and eight of eight responded to GA, GLA30, and GLAT, respectively, indicating a "breaking" of the tolerant state. This is in contrast to no reactors in the experimental group, but a significant number of reactors among the control animals after the first adjuvant injection of polymer.

The data also show that intravenous injection of polymer extended the state of immunological unresponsiveness in the rabbits that were treated initially with GA and GLA30. The quantitative differences in the antibody response in the various groups will be discussed in a subsequent publication. In general, however, significantly higher levels of antibody were produced in the control rabbits.

Thus, tolerance can be conferred by exposing newborn rabbits to antigenic synthetic polyamino acids. Tolerance has also been produced recently in rabbits toward two multichain polymers by Sela *et al.* (*9*; *10*).

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Prediction of the Comparative Reinforcement Values of Running and Drinking

Abstract. *The probability of free drinking and running in rats was controlled by sucrose concentration and force requirements on an activity wheel. Drinking and running were then made contingent on pressing a bar. Bar-pressing increased monotonically with the associated response probability, and equally for drinking and running. The results support the assumption that different responses of equal probability have equal reinforcement value.*

The reinforcement value of two different behaviors, running and drinking, may be compared despite their differences, with a model of reinforcement that (i) equates reinforcement value with response probability and (ii) treats the probabilities of different responses as commensurable magnitudes (*1*). Although comparing the strength of different drives and reinforcers has been a classical problem in psychology, progress has been slight. Early work by Warden (*2*), comparing the number of times that rats crossed an electrified grid for food, water, mate, and so forth, has been widely criticized, most constructively perhaps by suggesting that the same comparisons be made without shock. More recently, Guttman (*3*) has predicted that different sugars equated for sweetness on the basis of concentration will have equal reinforcement value. However, this kind of prediction is limited to stimuli located on a single dimension. Overcoming this restriction is a principal aim of my present work (*4*).

Consider that a rat, in separate operant drinking and running sessions, divides each session, on the average, between drinking and running, so that the estimated mean probabilities of drinking and running are both 0.5. According to the present model, if these behaviors are made contingent upon, for example, bar pressing, they will produce equal increments in probability. More generally, different responses of equal probability will have equal reinforcement value; when made contingent upon some less-probable response, they will produce equal increments in that response.

Testing this prediction requires establishing an overlapping range of probabilities (P) of free drinking (D) and free running (R) and then determining