tion. In either case the result of this genotypic alteration would be the development in the transformed cell of an antigen immunologically slightly different from the corresponding antigen in the normal cell.

1. Habel, K., Atanasiu, P., PROC. SOC. EXP. BIOL. AND MED., 1959, v102, 99.

2. Habel, K., Silverberg, R., *Virology*, 1960, v12, 463.

3. Law, L. W., Dawe, C. J., PROC. SOC. EXP. BIOL. AND MED., 1960, v105, 414.

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An Erythematous Disease of Adult Guinea Pigs Following Transplantation of Homologous Lymphoid Cells.* (26454)

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During studies on the transfer of delayed hypersensitivity to simple chemicals from highly sensitized to normal adult guinea pigs (1), occasional recipients of lymphoid cells developed an illness characterized by intermittent fever, squealing on handling, progressive weight loss, and generalized erythema. Evidence has now been obtained that this disorder is entirely independent of any artificial sensitization of the donor and may be produced with unprecedented high frequency by lymphoid tissue from a specific category of normal animals.

Following the discovery that certain guinea pigs possess natural, delayed type iso-hypersensitivity toward a heritable factor present in sera of other guinea pigs(2), an investigation was undertaken to determine whether a relationship might exist between this state of iso-hypersensitiveness and the illness following lymphoid cell transfer. As the following experiments show, the lymphoid tissue from guinea pigs lacking serum factor but possessing delayed iso-hypersensitivity toward it regularly induced the illness in adult recipients, while lymphoid tissue from guinea pigs possessing serum factor but lacking iso-hypersensitivity was incapable of inducing the disease.

The experimentally produced illness, which superficially resembles "runt", "homologous" and "secondary disease"(3-7), but which differs from them by its induction in normal non-inbred adults and by its characteristic erythema, has been termed "erythematous disease"(8,9). Certain features of erythematous disease recall and allow comparison with aspects of "parabiotic intoxication" or "parabiotic disease"(10,11).

Methods. Experiments concerned with inducing erythematous disease consisted of transplanting washed lymphoid cells from one or more donor guinea pigs into one or more recipients after testing each animal for serum factor and for iso-hypersensitivity to the factor.† Guinea pigs bred from Rockefeller Institute stock, weighing more than 400 g and kept in temperature controlled quarters, were used throughout. Presence or absence of serum factor was determined by injecting 0.1 ml of each animal's serum intracutaneously into separate "assay" guinea pigs of known dermal reactivity(2); an erythematous response greater than 10 mm in diameter at 24 hours was deemed positive for serum factor. Possession or lack of iso-hypersensitivity was ascertained on day of transplantation by observing an animal's cutaneous reaction to sera, known to contain serum factor(2), inoculated intradermally

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† Such tests, done to provide information for the matching of animals, are not necessary for induction of erythematous disease as the illness can be produced in animals that have not received any prior injection.

TABLE I. Induction of Erythematous Disease in Normal Adult Guinea Pigs by Lymphoid Cells from Donors Possessing Natural Delayed Type Iso-hypersensitivity (IH) and Lacking Serum Factor (SF).

	Donor		Recipient		Cell dose per recipient × 10^9	Recipients inoculated	Erythematous disease	Fatal erythematous disease	Day of death
	IH	SF	IH	SF					
A	+	—	—	+	1.4–2.2	6	4	2	18, 35
					1.8–2.2*	4	3	1	30
B	+	—	+	—	1.8–2.2	3	2	2	25, 37
					1.3–2.7*	5	3	2	26, 30
C	—	+	—	+	2.3, 3.4	2	0		
					1.4, 2.0*	2	0		
					4.0, 6.1†	2	0		
D	—	+	+	—	1.5, 3.3	2	0		
					1.5, 2.6*	2	0		
					4.0, 5.5, 6.1†	3	0		

* Pooled lymph node cells or spleen cells from 2 donors.
† " " " " " " " " 4-7 " .

(0.1 ml) one day earlier.† Guinea pigs with natural delayed type iso-hypersensitivity to homologous serum (and lacking the factor in serum responsible for eliciting dermal reactions) were used as donors in Exp. A and B (and as recipients in B and D) of Table I; animals lacking iso-hypersensitivity but possessing serum factor were used as donors in Exp. C and D and as recipients in A and C.

Certain recipients in each of the experimental groups received lymph node and spleen cells from a single donor; others received pooled lymph node cells or pooled spleen cells from 2 or more donors. Cells from "scissored" spleens and "teased" lymph nodes removed from exsanguinated guinea pigs were washed twice in Hanks' solution, passed through fine-mesh stainless steel collanders and inoculated intravenously or intraperitoneally (at times by both routes). Small samples of cells were reserved for counts in a haemocytometer; viability, judged by vital staining with trypan blue, was 80-90%.

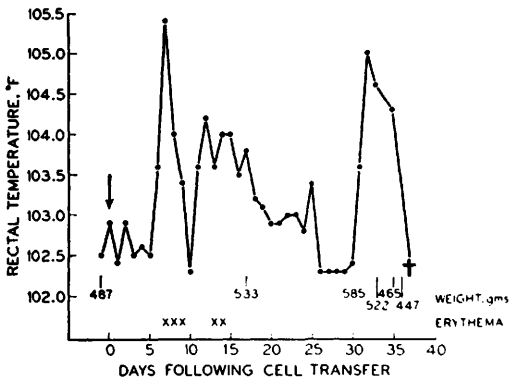

FIG. 1. Erythematous disease in a guinea pig (from Exp. B of Table I). Arrow marks receipt of 1.8 × 10^9 lymph node and spleen cells; generalized erythema (×) occurs at and following peaks of fever; wt loss is terminal (in other animals it may begin earlier).

Results. That lymphoid cells from guinea pigs lacking serum factor but possessing iso-hypersensitivity toward it are capable of inducing erythematous disease in normal adult recipients is obvious from Exp. A and B, Table I. Cells from such donors induced an illness marked by intermittent fever, weight loss and erythema in 12 of 18 recipients, 7 of which died within 18-37 days.‡ As few as 1.4-2.2 × 10^9 cells from a single donor sufficed to bring about the illness, a typical course of which is shown in Fig. 1. In contrast, lymphoid cells from donors lacking iso-hypersensitivity but possessing serum factor (Exp. C and D) failed to induce the illness in 13 recipients, although as many as 4.0-6.1 × 10^9 cells from 4-7 donors were inoculated into some of the animals.

A suggested basis for the ability of lymphoid cells from animals with iso-hypersensitivity and lacking serum factor to induce erythematous disease might be that such cells have, through reactivity to serum factor, an immunological advantage over their hosts.

‡ Liver cells, erythrocytes and sera of animals with effective lymphoid cells were unable to initiate the disease.

TABLE II. Rejection of Skin Homografts in Normal Adult Guinea Pigs Possessing or Lacking Delayed Type Iso-hypersensitivity (IH) and Serum Factor (SF).

Donor		Recipient			
IH	SF	IH	SF	No. grafts	Graft survival (days)
+	—	—	+	4	13
+	—	+	—	11	13–15
—	+	—	+	22	13–17
—	+	+	—	4	9–14

This mechanism might conceivably account for the high incidence of the disease in recipients with serum factor (Exp. A); however, it could not account for the equally high incidence of the disease observed in recipients lacking serum factor and possessing iso-hypersensitivity (Exp. B; Fig. 1). An alternative basis for a "graft-versus-host" mechanism would be provided if the effective lymphoid cells (which are from animals genetically lacking serum factor) were for some reason selectively tolerated by the recipient hosts. However, in an experiment in which full thickness (1 cm^2) skin grafts were exchanged among guinea pigs of Rockefeller Institute stock, matched for possession or lack of serum factor and iso-hypersensitivity, no immunological tolerance to homologous tissue was detected (Table II). Thus, all skin homografts were rejected within a time range (9-17 days) not far removed from that which others have noted for first-set homografts (12); whereas, a majority of autologous (control) grafts appeared well seated and healthy at 22 days and beyond.

The possibility that some mechanism other than graft-versus-host reaction may be responsible for erythematous disease is being explored.

Summary. Adult, immunologically competent, non-inbred guinea pigs injected with selected homologous lymphoid cells develop a wasting, sometimes fatal illness. Termed "erythematous disease," it is induced by spleen and lymph node cells from guinea pigs lacking heritable serum factor toward which they possess naturally occurring delayed type iso-hypersensitivity.

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1. Battisto, J. R., Chase, M. W., *Fed. Proc.*, 1955, v14, 456.
2. Battisto, J. R., *Nature*, 1960, v187, 69.
3. Billingham, R. W., Brent, L., *Transpl. Bull.*, 1957, v4, 67.
4. Cole, L. J., Ellis, M. E., *Science*, 1958, v128, 32.
5. Simonsen, M., *Acta Path. Microbiol. Scand.*, 1957, v40, 480.
6. Trentin, J. J., *Fed. Proc.*, 1958, v17, 461.
7. Schwartz, E. E., Upton, A. C., Congdon, C. C., PROC. SOC. EXP. BIOL. AND MED., 1957, v96, 797.
8. Battisto, J. R., *Bact. Proc.*, 1960, 86.
9. ———, *Ann. N. Y. Acad. Sci.*, 1960, v87, 468.
10. Herrmannsdorfer, A., *Deutch Z. für Chir.*, 1923, v178, 289.
11. Nakic, B., Silobrcic, V., *Nature*, 1958, v182, 264.
12. Bauer, J. A., Jr., *Ann. N. Y. Acad. Sci.*, 1958, v73, 663.

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A Simple, Rapid Skin-Graft Technic in Rats. (26455)

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A modification of the punch technic for skin grafting as performed on mice(1,2) has been successfully adapted to rats. Improvements developed during studies on 242 rats have resulted in a regularly obtained healthy skin graft. Sutures are unnecessary in this technic. In mice a tape vest can be used(3), but because of the greater strength of rats, we have found it necessary to use a plaster jacket. The graft is well immobilized in a