The high ratio of I^{125}/Cr^{51} in the thymus could mean that a population of phagocytic cells inefficient in uptake of Cr^{51} migrates preferentially into the thymus. This possibility seems unlikely since it is known that free Cr^{51} after i.p. injection into mice distributes equally into different organs[4]. Alternative explanations are that a small population of PEC takes up I^{125}cBSA quickly, or stores it efficiently, or that the thymus provides macrophages with a favourable environment for retaining antigen.

It is known from studies using S^{35}-BSA that antigen can enter and is retained in the thymus[5]. Macrophages have also been observed in the thymus[6], where in part they may act as scavangers; but they have also been found in close contact with lymphocytes in mitosis within the thymus of AKR mice[7]. It is concluded from the experiments reported in this communication that efficient presentation of antigen to thymus lymphocytes by other cells may be a part of the normal immune response[10].

Zusammenfassung. Makrophagen aus dem Peritoneum von CBA-Mäusen, die in Zellkultur hitzedenaturiertes Rinder-Serumalbumin phagozytiert haben, transportieren dieses bis zu 4 h nach Transplantation vornehmlich in den Thymus normaler Empfängertiere.

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[4] P. V. Vittorio, E. W. Wight and B. E. Sinnott, Can. J. Biochem. Physiol. *40*, 1677 (1962).
[5] J. S. Garvey, D. V. Eitzman and R. T. Smith, J. exp. Med. *112*, 533 (1960).
[6] J. N. Blau, Nature *208*, 564 (1965).
[7] D. Metcalf and M. Ishidate, Aust. J. exp. Biol. med. Sci. *40*, 57 (1962).
[8] A. S. McFarlane, Nature *182*, 53 (1958).
[9] B. Benacerraf, G. Biozzi, B. N. Halpern, C. Stiffel and D. Mouton, Br. J. exp. Path. *38*, 35 (1957).
[10] I thank Drs. D. W. Dresser and N. A. Mitchison for stimulating criticism. This work was partly supported by a Fellowship of the Royal Society European Programme.
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Transvascular Passage of Albumin-I^{131} into Skin of Immunized Mice

It is possible that changes in the connective tissue-interstitial space may affect the manner and the rate of transport of molecules to and from the circulatory system and the cells. It has been proposed that this sequence may play a significant role in aging and that the connective tissue changes may result from genetically programmed chronogenic phenomena and exogenously derived pathogenic alterations[1]. Among the latter are immunologic processes. Antigen-antibody interactions are known to occur in the interstitial space and in basement membranes[2]. These interactions and their sequalae might result in alterations in the diffusibility characteristics of the milieu through which molecules must pass on their way to and from the cells. This study was undertaken in order to test this hypothesis.

Method. Male mice weighing 28 ± 1 g were obtained from a commercial supplier and maintained on Purina pellets. 1 group of animals was injected s.c. with 0.5 ml of a 5% solution of sodium caseinate, 5 times a week for a period of 6 weeks according to the procedure of Christensen and Hjort[3]. Each animal received a total of 750 mg of sodium caseinate. Another group received a s.c. injection of 0.2 ml streptococcus group A extract (BBL-74027B) in complete Freund's adjuvant and 0.1 ml of the soluble antigen i.p. 4 weeks later.

48 h following the last injection of sodium caseinate, and 2 weeks after the last injection of streptococcal antigen, these animals and their controls were injected in a tail vein with 1 μc of human albumin-I^{131} in a volume of 0.1 ml. In some animals, after 4 min and in others after 2 h, samples of blood were obtained from the internal occular plexus and the mice were killed by cervical fracture. The skin was removed in a uniform manner, dehaired, scraped free of s.c. tissue, dissolved in formic acid, and assayed for bound I^{131}, as previously described[4]. 0.02 ml of serum was used for I^{131} assay.

Results and discussion. The results are shown in the Table. As in the previous experiments[4], the 4 min values were assumed to correspond to the mixing time in the plasma and the radioactivity in the skin was thought to be due to the circulating plasma.

The mean plasma volumes in the skin calculated from 4 min values were 0.0309 ml, 0.0411 ml and 0.0435 ml, respectively, in the control, casein- and strep-antigen treated animals. After 2 h, the serum radioactivity decreased to 64.2%, 77.9% and 91.5%, respectively, of the

Albumin-I^{131} in serum and skin of immunized mice

	No.	Weight (g)	Serum (cpm 0.02 ml)	Skin (cpm total)
4 min				
Control	8	39.2	11990 ± 947[a]	18561 ± 2061
Casein	8	29.8	10026 ± 793	20623 ± 1037
Strep-antigen	7	34.3	8537 ± 1039	18589 ± 1872
2 h				
Control	8	39.5	7695 ± 514	27173 ± 1678
Casein	8	29.1	7810 ± 520	30027 ± 1101
Strep-antigen	7	34.7	7808 ± 320	29023 ± 2451

[a] Standard error of the mean.

[1] H. Sobel, Adv. Geront. Res. *2*, 205 (1967).
[2] F. J. Dixon, in *Mechanism of Cell and Tissue Damage Produced by Immune Reactions* (Ed. P. Grabar and P. Miescher; Grune and Stratton, Inc., New York 1961), p. 71.
[3] H. E. Christensen and G. H. Hjort, Acta path. microbiol. scand. *47*, 140 (1959).
[4] H. Sobel, K. Fard and T. Robuck, Proc. Soc. exp. Biol. Med. *123*, 519 (1966).

4 min values. On the assumption that the plasma volume in the skin did not change during the 2 h interval, the radioactivity due to the transvascular-passed albumin-I^{131} in this organ was calculated. These values were 15,285 cpm, 13,977 cpm and 12,041 cpm, respectively. This indicates that the transvascular-passed labeled albumin of the experimental groups compared to the normal control is 91.4% for the amyloidic and 78.8% for the strep-antigen group. Thus, the data suggest that plasma clearance is delayed and transvascular passage of the labeled albumin into the skin is reduced at 2 h. Since the radioactivity in the sera of immunized animals at 2 h is even slightly higher than that of the normal control, any uptake of the radioactivity from the pool by other organs could not have decreased the transvascular passage of albumin-I^{131} into the skin. The results are consistent with the original hypothesis that immunization may have affected the architecture of the interstitial space-ground substance[5].

Zusammenfassung. Mäuse wurden mit Kasein- und Streptokokkus-Antigen injiziert. In den immunisierten Tieren ist die Ausscheidungsgeschwindigkeit von i.v. injiziertem Albumin-I^{131} aus dem Plasma erniedrigt, und ebenso ist im Vergleich zu den Kontrolltieren der transvaskuläre Transport in die Haut reduziert.

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An Attempt at Colonization of W^vW^v Anemic Mice by Rat Hemopoietic Tissue

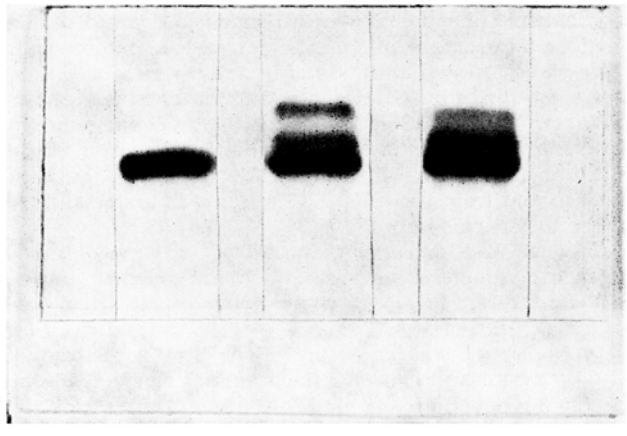
Anemic mice of the W series can be transplanted with normal mouse hemopoietic tissue. BERNSTEIN and RUSSELL[1] showed that syngeneic tissue would implant without previous irradiation of the host, and SELLER and POLANI[2] later used allogeneic tissue. This was administered during the immediate neonatal period before immunological competence is established. Red cells of donor origin could be demonstrated in the circulation of the transplanted animals for the rest of their lives[3], and when hemopoietic tissue bearing chromosome markers was used, the donor cells could be directly observed in the host[4].

In irradiation experiments in mice, hemopoietic tissue is administered to circumvent the death which normally follows a high dose of irradiation. It has been shown that this is effective not only with mouse hemopoietic tissue but also with rat[5] and hamster[6] tissue. Recovery, although often only temporary, was due to repopulation of the host by the donor tissue[7].

Thus, if the immunological barrier is overcome and the environmental conditions in the host are suitable, hemopoietic tissue from one species will live and proliferate in a member of another species. It was wondered whether rat hemopoietic tissue would implant in the W series anemic mice following administration immediately after birth. If successful, ways would exist for testing the chimerism established which are not available when mouse hemopoietic tissue is used.

The method used was as previously described[2]. A suspension of liver cells obtained from 19- to 20-day-old foetal Wistar or Sprague-Dawley rats was injected i.v. into mice of the genotype W^vW^v within the first day of life. When these animals were adult, various studies were made on them for evidence of implantation of the rat hemopoietic tissue. Red blood cell counts were made by conventional hemacytometry, using Hayem's fluid as the diluent. The hemoglobins were studied by electrophoresis on cellulose acetate paper, as previously described[3]. The presence or absence of alkaline phosphatase activity in the granulocytes was detected histochemically on blood smears[8]. Plasma proteins were separated by electrophoresis on a horizontal starch gel according to the method of SMITHIES[9].

Initially 10 to 12×10^6 rat foetal liver cells were injected into the new-born W^vW^v recipients, but no evidence of implantation was observed in the first 6 treated mice which survived to maturity. Experiments on the induction of tolerance to foreign tissue in mice suggest that the wider the antigenic disparity between the donor and the host, the greater the number of cells



Electrophoresis on cellulose acetate paper of hemoglobins of a W^vW^v mouse, a rat and a W^vW^v mouse successfully transplanted with rat hemopoietic tissue.

[1] S. E. BERNSTEIN and E. S. RUSSELL, Proc. Soc. exp. Biol. Med. *101*, 769 (1959).
[2] M. J. SELLER and P. E. POLANI, Nature *212*, 80 (1966).
[3] M. J. SELLER, Nature *212*, 81 (1966).
[4] M. J. SELLER, in preparation.
[5] C. W. CONGDON and E. LORENZ, Am. J. Physiol. *176*, 297 (1954).
[6] D. W. VAN BEKKUM, Nature *202*, 1311 (1964).
[7] R. C. NOWELL, L. J. COLE, J. G. HABERMEYER and P. L. ROAN, Cancer Res. *16*, 258 (1956).
[8] Sigma Technical Bulletin No. 85.
[9] O. SMITHIES, Biochem. J. *61*, 629 (1955).