Table II. Effect of epinephrine on muscle phosphorylase activity in normal, BPV, prednisolone and BPV + prednisolone-treated rats

	Phys. saline		Epinephrine	
	Active phosphorylase mmol $P_i/g'^2\,h^{-1} \pm$ SE	a/T [a]	Active phosphorylase mmol $P_i/g^2'h^{-1} \pm$ SE	a/T [a]
Normal	1.53 ± 0.18	0.27 ± 0.03 (9)	2.73 ± 0.24	0.45 ± 0.05 [b] (9)
BPV	1.72 ± 0.15	0.29 ± 0.03 (7)	1.92 ± 0.16	0.33 ± 0.04 [c] (7)
Prednisolone	2.43 ± 0.20	0.32 ± 0.05 (7)	4.71 ± 0.29	0.58 ± 0.06 [b] (7)
BPV + Prednisolone	2.13 ± 0.28	0.32 ± 0.04 (7)	3.83 ± 0.31	0.52 ± 0.06 [b] (7)

[a] Ratio of active to total phosphorylase activity [b]. $p < 0.01$ related to values obtained after phys. saline. [c] $p < 0.01$ if the increase caused by epinephrine in normal animals was related to that of detected in BPV-treated rats. Numbers in parentheses represent the number of animals in each group.

of the sequential steps involved in the conversion of inactive to active phosphorylase. Previous experiments regarding the disturbed insulin secretion [5] and the inhibited hyperglycemic response to cyclic AMP [7] in BPV-treated rats indicate that adenylcylase is not depressed by BPV. Since it is known that insulin [8] and adrenalectomy [9] elevate the activity of cyclic AMP phosphodiesterase, besides other possibilities, an increase of phosphodiesterase activity caused by elevated plasma insulin [7] and by decreased blood cortiocosterone level [10] of BPV-treated animals could be taken into account.

Prednisolone restored the ability of epinephrine to induce hyperglycemia [2] and to activate glycogen phosphorylase. Its inhibitory effect on phosphodiesterase activity [9] may play a role in the restoration of sensitivity to epinephrine in BPV-treated animals. Naturally, there are other possibilities, too. Further experiments will have to be carried out to elucidate this problem.

Zusammenfassung. Die Glycogen-Phosphorylase-aktivierende Wirkung von Epinephrin wurde in Lebern und Muskeln von Ratten durch BPV-Behandlung gehemmt und die Epinephrinempfindlichkeit der BPV-behandelten Tiere durch Prednisolon wiederhergestellt.

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Erythrocyte Chimaerism in *W*-Series Anaemic Mice after Allogeneic Splenic Transplants to the Renal Cortex

Anaemic mice of the genotype W^vW^v have a genetically determined, lifelong, normochromic, macrocytic anaemia, which does not respond to therapy with iron or liver extract [1], folic acid or vitamin B12 [2]. Such mice can however, be cured by the administration of a cellular suspension of normal haemopoietic tissue [3, 4], usually derived from the foetal liver or adult bone marrow.

In the mouse, although the spleen is intimately involved in the lymphoid system it is also an erythropoietic organ [5, 6]. In the present work, a portion of whole spleen from a haematologically normal mouse is transplanted to the renal cortex of W^vW^v mice. It is found that stem cells emanate from this graft, proliferate and supplant the defective host's bone marrow, and permanently cure the animal.

Table I. Mean red blood cell count/mm$^3 \times 10^6$ of W^vW^v mice treated with ALS or NRS before and after receiving a solid tissue graft of spleen from haematologically normal mice

Number of mice	Serum Treatment	Day 0	40	80	120	200
9	ALS	6.7	10.3	10.3	11.1	10.7
10	NRS	6.8	7.7	7.1	6.9	7.1

Adult anaemic W^vW^v mice were used as the recipients. The spleen donors were a pure line CBA-H strain. They have a different haemoglobin from the *W* mice, and possess the T6 chromosome markers. This permitted the identification of the donor cells in the hosts. Skin grafts exchanged between the two strains were rejected in approximately 11 days, indicating a strong histocompatibility difference, thus necessitating immunosuppression for survival of the spleen grafts. Antilymphocytic serum (ALS) was used for this purpose and was prepared in rabbits as previously described [7].

W^vW^v mice were injected i.p. with 0.25 ml of ALS each morning for 5 consecutive days. Control mice received the same amount of decomplemented normal rabbit serum (NRS). On the afternoon of the 5th day, approxi-

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mately $^1/_3$ of a donor spleen was transplanted to a bed prepared in the renal cortex by the method of WHEELER, CORSON and DAMMIN[8]. ALS or NRS was administered 3 times during the 1st post-operative week, twice in the 2nd week, and once during the 3rd week.

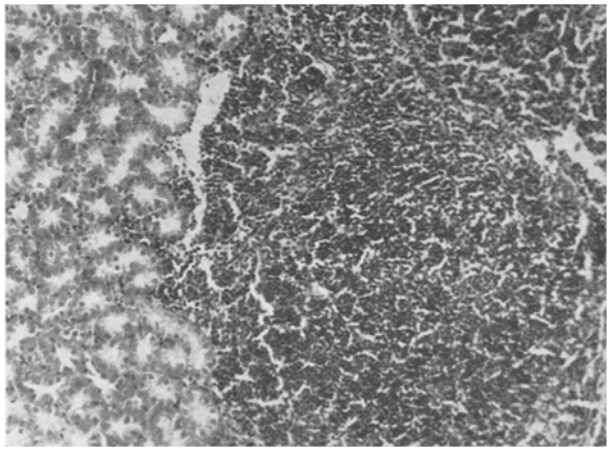
Red blood cell counts made by routine haemacytometry, and electrophoresis of the haemoglobins from red cell lysates[9] were performed on day 0, before transplantation, and on days 40, 80, 120 and 200 after grafting. After day 200, chromosome studies of various tissues were made using the air drying method of FORD[10]. In some cases the spleen graft was examined cytologically and in others its histology was studied after sectioning and staining with haematoxylin and eosin.

Nine of the 14 mice (64%) treated with ALS and an allogeneic solid tissue spleen graft showed an increased red blood cell count (Table I) together with the presence of donor haemoglobin. It was first apparent on day 40 and was maintained through to day 200 when the experiment was terminated. None of the control NRS treated mice showed any increase in red cell numbers or the presence of donor type haemoglobin.

Table II. Mean percentage of donor cells in the tissues of W^vW^v anaemic mice 200 days after being transplanted with a solid tissue graft of haematologically normal spleen

% Donor cells found in				
Bone marrow	Spleen	Thymus	Lymph nodes	Spleen graft[a]
99	98	96	74	95

[a] 50 or 100 metaphase plates scored in each tissue.



Histological appearance of part of a healthy spleen graft from a haematologically normal mouse 200 days after transplantation to the renal cortex of a W^vW^v anaemic mouse. Kidney on the left, part of the spleen graft on the right. ×187.

Chromosome studies made after day 200 showed that donor cells comprised almost the whole of the dividing population of the W^vW^v bone marrow and also the spleen and thymus and much of the lymph nodes (Table II). Interestingly, the spleen graft itself did not consist entirely of its original CBA cells but in all cases it contained some W cells, emphasizing the free circulation of haemopoietic stem cells between the components of the lympho-myeloid complex.

Macroscopically, the successful spleen grafts resembled an intact spleen. They had not increased in size since grafting. Microscopically, they showed the normal splenic architecture of trabeculae, splenic nodules and red pulp (Figure). There was no obvious sign of erythropoiesis taking place. In all the control mice there was no spleen apparent to the naked eye, but a whitish layer covered the graft bed. There was no regeneration of the kidney, the bed remaining as an indentation in the cortex. Microscopically, there was a thin eosinophilic layer next to the kidney tissue, acellular except for a few mononuclear cells. On the outer side of this there was a fairly thick layer of connective tissue.

Although the adult spleen is regarded mainly as a lymphopoietic organ, HELFRE et al.[11] found that there is an erythroblastic line amounting to about 5% of the total cellular output. However, it is shown by the identification of the donor cells in some of the recipient organs that the W^vW^v mice become cured of their anaemia not by the grafted spleen becoming an erythropoietic organ, but by the migration of stem cells from the graft to the bone marrow. Some implant there, multiply and replace the defective W^vW^v cells and institute normoblastic erythropoiesis[12].

Résumé. Une portion d'une rate allogénique normale été transplantée sur le rein de souris anémiques, génotype W^vW^v, immunosuppressent avec le sérum antilymphocyte; 64% ont guéri. Les cellules hématopoïétiques émigrent hors de la greffe dans la moelle osseuse, s'y fixent, prolifèrent et remplacent les cellules défectueuses de l'hôte.

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Brain Norepinephrine Levels and Turnover Rates in Castrated Mice Isolated for 13 Months[1]

Environmental isolation is known to induce behavioral changes in both animals[2,3] and man[4,5]. One such change is the increased aggressiveness observed in a number of strains of adult male mice following isolation[6–8]. The presence of testosterone, the male sex hormone, appears necessary for the occurrence of this phenomenon in mice. For example, isolation-induced aggression can be prevented if mice are castrated prior to isolation[9]. Steroid replace-