into normal DBA/2 animals. This is an illustration that factors associated with tissue rejection are not identical with the components of the classical immune mechanism.

Summary. 1. A strain of mice resistant to the transplanted CD/5 lymphoma (DBA/2), and a tumor susceptible strain (BALB/C), were rendered mutually graft-tolerant by neonatal cross-immunization with spleen cells. At 6-8 weeks mice of both strains were injected subcutaneously with CD/5 lymphoma, which is isologous in BALB/C mice. Growing tumors in BALB/C mice were then challenged by an "adoptive" immunization procedure using spleen and lymph nodes from resistant DBA partners. 2. Neo-natally cross-immunized BALB/C mice were more resistant (45%) to the tumor than control animals (13%). 3. Following adoptive immunization, complete tumor regression was observed in 20% and partial regression in 25% of tumor bearing animals. Corresponding figures for a control group of normal BALB/C subjected to the same adoptive immunization were: complete regression (0%), partial regression (8%). 4. Antibody titers in DBA/2 mice against tumor protein did not correlate with tumor rejection. Neo-natally cross-immunized DBA/2 mice were less resistant to tumor (91%) than normal DBA/2 (100%). Antibody titer was minimal or absent in tumor resistant DBA/2 mice, but high in those cross-immunized mice accepting the tumor.

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Received June 24, 1963. P.S.E.B.M., 1964, v115.

Circulatory Effects of a Homologous Plasma-Blood Exchange in the Dog.* (28823)

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Bliss *et al*(1) first reported that intradermal injection of homologous plasma produced well marked wheals in dogs. Infusion of homologous plasma into normovolemic dogs produced the following symptoms: a fall in blood pressure, skin edema, labored respiration, prolonged bleeding time and death of a majority of dogs within a 24-hour period. Also, the dogs did not retain the infused fluid and protein within the circulation. None of these reactions occurred when autologous blood and plasma were infused. These various responses were suggestive of a foreign protein reaction, and because they occurred with the infusion of homologous plasma as well as blood, it was suggested that an unknown "plasma factor" must be the inciting agent(1-3).

Hypervolemia, which occurred with the previous experiments, was avoided by Lawson *et al*(4) by simultaneously withdrawing a volume of blood equivalent to that infused. Under these circumstances, when autologous plasma was used for the exchange, the distribution spaces of the dye T-1824 and P^{32}-tagged erythrocytes agreed with those calculated from the dilution of the tags by the exchange. When autologous blood was transfused to increase the blood volume of normovolemic dogs, the agreement for the cell vol-

This study was supported in part by Medical Research and Development Board, Office of Surgeon General, Dept. of the Army, and in part by a grant from Nat. Heart Inst., USPHS.

ume was good, but large differences occurred between plasma volumes determined initially by T-1824 and those calculated subsequently from the dilution of the tag.

Contrary to these data, when dogs were rendered hypovolemic, plasma volume restoration occurred equally well whether homologous or autologous plasma was used. Further, only 2 of the 19 dogs developed wheals, and these were minor in character (5).

To test these reported differences, an experiment was devised using dogs in which homologous plasma was exchanged for blood so that the blood volume was not expanded.

Materials and methods. Seven dogs were anesthetized with 10 mg/kg of morphine sulfate subcutaneously followed by 15 mg/kg of sodium pentobarbital in 20 to 30 minutes. The routine procedures used in this laboratory for this type of experiment have been reported(6). Cell and plasma volumes were determined by Cr^{51} tagged red cell and T-1824 dye dilution methods, respectively(7, 8). Specific gravity of the plasma proteins was determined on all samples by the falling drop method(9), and from these data the protein concentration was calculated. The hematocrit was measured in Wintrobe blood index tubes centrifuged at 2,500 rpm for 20 minutes and corrected by 0.95 for the trapped plasma. Blood samples were taken by catheter from the right atrium at 10, 20 and 30 minutes after injection of the tagging materials. Carotid arterial pressure was measured with a mercury manometer. After the samples for the control determinations had been drawn, the dogs were bled from the left femoral artery and plasma from a donor dog was infused simultaneously through the right femoral vein. The rate of the exchange was so regulated that the rate of blood removed was the same as the rate of plasma infused, thus blood loss equalled plasma gained. The volume of the exchange varied from 40 to 50 ml/kg with a mean volume of 44.0 ml/kg. Cell and plasma volume, hematocrit and protein determinations were made after the blood plasma exchange. Samples were taken at 10, 20, 30 and 60 minutes after the dye and tagged red cell injections. Then the tube leading to the bleeding bottle was reopened and the dogs were bled slowly to a mean arterial pressure of 35 mm Hg. When the mean arterial pressure of the dog fell below 35 mm Hg, the tube was clamped and the final measurements were made.

Results. The exchange was accomplished with only a small decrease in mean arterial pressure from the control level of 101 to 91 mm Hg. However, one dog, not included in the mean value, had a precipitous fall in pressure. After the exchange the agreement between the measured and expected plasma and cell volume, protein concentration was very good. As a result of the exchange of plasma for blood, the venous hematocrit fell from 42.4 to 23.9%, the circulatory hematocrit from 36.8 to 19.3%, and the BVR_{cells} (circulatory hematocrit/venous hematocrit) decreased from 0.87 to 0.80 (Table I).

Then the dogs were bled slowly to a mean arterial blood pressure of 35 mm Hg. The mean bleeding volume to reach this pressure was 23 ml/kg, and represented 30% of the measured blood volume. Contrary to our usual experience, the blood pressure tended to fall progressively during the final determinations. The blood volume after the hemorrhage was significantly less than expected because 5.9 ml/kg of plasma apparently left the circulation. At the same time there was a loss of 0.46 g/kg of protein reducing the concentration from an expected 5.25 to a measured 5.08 g/100 ml. The concentration of protein leaving the circulation was 7.8 g/100 ml of plasma.

Discussion. Depending on the experiment, the infusion of homologous plasma or blood results in effects different than those obtained with autologous plasma or blood(2-5). The present experiment, with some modifications, is similar to one reported by Lawson *et al* (4), in which they utilized the principle of exchanging the blood of a dog for either homologous or autologous blood or plasma. However, the plasma used for the autologous experiment was contaminated, as they point out, by as much as 50% of homologous plasma. In spite of this, they found that with this so-called "autologous" plasma infusion the distribution space of T-1824 agreed with

the space calculated from the infused unlabeled plasma. This agreement did not occur if only homologous blood or plasma was infused. However, when the blood volume of normovolemic dogs was expanded with autologous plasma, there was a discrepancy between the volume distribution of the infused, unlabeled plasma and T-1824 dye, although this experiment, too, was complicated by the use of homologous blood to replace autologous blood in order to maintain the original blood volume.

In our initial experiment, which was comparable to their exchange experiment with homologous plasma, both the measured cell and plasma volumes agreed well with the expected volume. The latter was calculated from the initial measurements and the red cells and plasma removed from and added to the circulation with the exchange. Further, none of the dogs developed reactions attributed to homologous blood or plasma by various investigators, although during the years we have observed in this laboratory that about 10% of the dogs overtransfused with homologous blood developed a mild urticaria. Therefore, it was found that homologous plasma successfully replaced the dogs' plasma removed during the exchange, and it can be concluded that under these experimental conditions homologous plasma does not produce any effect other than would have been expected with autologous plasma.

However, there were striking differences between these dogs subjected to a blood-homologous plasma exchange and control dogs subjected to hemorrhage. From previous data, for example, when dogs were bled to 35 mm Hg, the mean bleeding volume was 46% of initial blood volume, and 7 ml/kg of fluid was added to the circulation with a mean protein content of 3.2 g/100 ml(10). The dogs in the present experiment, on the contrary, bled only a mean of 30% of their blood volume to reach an arterial pressure level of 35 mm Hg. Plasma volume and total protein, were less instead of greater than expected, because 5.9 ml/kg of plasma and 0.46 g/kg of protein have left the circulation.

These data show that the exchange of ho-

TABLE I. Plasma-Blood Exchange Followed by Hemorrhage to 35 mm Hg Mean Arterial Pressure.

	Venous hematocrit, %	Plasma vol, ml/kg	Cell vol, ml/kg	Blood vol, ml/kg	Circulatory hematocrit, %	BVR_{cells}	Plasma proteins g/100 ml	Plasma proteins g/kg
Control	42.4 ± 3.36*	54.2 ± 6.84	29.6 ± 1.59	83.7 ± 6.44	36.8 ± 3.68	.87 ± .05	5.51 ± .24	2.90 ± .30
Blood lost†	31.0 ± 2.44	33.5 ± 2.00	15.0 ± .87				5.55 ± .19	1.86 ± .10
Plasma infused		44.0 ± 1.62					5.48 ± .28	2.42 ± .16
Expected after exchange		64.8 ± 5.59	14.6 ± 1.50	79.4 ± 5.80	18.7 ± 2.15		5.43 ± .24	3.46 ± .26
Measured after exchange	23.9 ± 1.99	63.0 ± 5.80	14.6 ± 1.39	77.6 ± 6.73	19.3 ± 2.80	.80 ± .05	5.49 ± .21	3.42 ± .29
Hemorrhage blood	23.9 ± 2.24	17.5 ± 2.46	5.5 ± 1.28	23.0 ± 3.57			5.60 ± .35	.98 ± .11
Expected after hemorrhage		45.5 ± 5.89	9.1 ± .91	54.6 ± 6.37	18.5 ± 3.46		5.25 ± .26	2.44 ± .35
Measured after hemorrhage	21.2 ± 1.58	39.6 ± 5.30	8.8 ± .47	48.4 ± 5.26	19.8 ± 3.24	.91 ± .09	5.08 ± .27	1.98 ± .24

* Mean values for 7 dogs with a mean wt of 11.4 ± .38 kg.

† These values include samples withdrawn.

mologous plasma for the animal's blood before the hemorrhage has in some unknown manner both reduced the bleeding volume and prevented the usual movement of fluid and protein into the circulation accompanying a hemorrhage to 35 mm Hg arterial pressure. There is no evidence that the same results might not have been obtained if autologous plasma had been used for the exchange. Unfortunately, neither the present experiments nor those of Lawson *et al*(4) permit even tentative conclusions concerning the mechanism producing this effect.

After hemorrhage, in spite of plasma leaving the circulation, the venous cell percentage decreased while the circulatory hematocrit did not change. Thus, it may be assumed that plasma from the small vessels or low hematocrit compartment entered the large vessel system or high hematocrit compartment(11). Consequently, the BVR_{cells} increased from 0.80 after the plasma-blood exchange to 0.91 after the hemorrhage.

Summary. The effect on plasma and red cell volume and protein concentration of exchanging homologous plasma for the dogs' own blood before a hemorrhage to 35 mm Hg mean arterial pressure was tested in anesthetized dogs. The measured cell and plasma volumes and protein concentration were in good agreement with those expected after the exchange. Therefore, homologous plasma successfully replaced the dogs' plasma removed during the exchange, and no reaction was seen attributable to the plasma infusion. When these animals were subjected to hemorrhage, the mean bleeding volume was 30% to reach a level of 35 mm Hg arterial pressure in contrast to 46% for dogs not receiving an exchange. Also 5.9 ml/kg of plasma and 0.46 g/kg of protein has escaped from the circulation while previously there was mobilization of fluid and protein after a hemorrhage.

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Received June 26, 1963. P.S.E.B.M., 1964, v115.

Some Characteristics of a Proteolytic System from *Phymatotrichum omnivorum.**† (28824)

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The importance of *Phymatotrichum omnivorum* (Shear) Duggar as a plant pathogen has prompted extensive investigations of this fungus from morphological, physiological, and agronomic standpoints. Little consideration, however, has been given to the study of the enzymes produced by this organism. As part of a fundamental investigation of the metabolism of *P. omnivorum,* we have determined some characteristics of proteolytic systems found in culture filtrates from 2 pathogenic strains. The existence of proteinase ac-

* Supported in part by grants from U. S. Public Health Service and Robert A. Welch Foundation.

† Contribution of Texas Agri. Exp. Station.

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