I and II contained antibody fragments I and II, respectively; antibody fragment III was found in fraction III. Fractions I and II also contained ovalbumin that reacted with rabbit antibody to ovalbumin, most of it being in I; in fraction III none was evident by the precipitin method, although a trace was detected with the more sensitive complement fixation method. The ovalbumin was unquestionably bound to antibody fragments I and II because it migrated electrophoretically with these. An antigenic constituent of human serum was present only in fraction II obtained from the specific precipitate formed in the presence of fresh human serum, an indication that the antigen was a component of C′. Its electrophoretic mobility was the same as that of antibody fragment II, but it could not be concluded on the basis of this finding alone that C′ was bound to fragment II in the water-soluble fraction because the known antigenic components of C′ and fragment II normally have similar β-mobilities.

Analysis of the saline-soluble fraction from the precipitate formed in the presence of fresh human serum showed only antibody fragments I and II and constituents of human serum (Figs. 1 and 2). The presence of fragment III was excluded because no component with its characteristic slow electrophoretic mobility was ever found in it.

No constituents of human serum were present in the control preparations in which heat-inactivated human serum or saline had been used, an indication that the antigens of fresh human serum precipitated with antigen-antibody were components of C′. The concentrations of antibody fragments I and II were greater in the water-insoluble fraction from the preparation containing human C′ than in those with heat-inactivated C′ or saline. This result could have been and very likely was due to the fixation of water-insoluble components of C′ to antibody fragments; antigenic components of C′ were found predominantly in the water-soluble fraction (Fig. 2).

These results show that C′ is not bound to fragment III because fragment III was never found in any fraction containing antigens of fresh human serum fixed by the specific precipitate. Rather, the results suggest that components of C′ are complexed to fragments I and II. This conclusion is consistent with the very recent findings of Schur and Becker (*7*) that 5*S* antibody fragments of rabbit and sheep antibody, which apparently lack fragment III, do fix C′ significantly when washed specific precipitates are used.

Our conclusion that C′ is not fixed to antibody fragment III in the normal course of complement fixation may be reconciled with the observations that fragment III inhibits immune hemolysis and that heat-aggregated fragment III fixes complement by assuming that fragment III is primarily involved in a possible activation step which must take place before actual fixation of complement to antibody-antigen aggregates can occur. Alternatively, it may be that the action of papain-cysteine differs, depending upon whether the antibody is in its native state or is part of a specific precipitate, in which case it is possible that the portion of fragment III that fixes complement goes with fragment II or fragment I when the specific precipitate is digested (*8*).

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Dissociation of Homograft Response to Allogeneic versus Xenogeneic Skin Grafts in Irradiated Mice

Abstract. *Lethally x-irradiated (C3H × DBA/2)F₁ mice were protected with syngeneic (isogenic) bone marrow and/or prior treatment with urethan and skin grafted at various times after irradiation. The ability to reject a first-set xenogeneic (heterologous) skin graft with normal vigor returned within 92 days; the first-set response to allogeneic (homologous) grafts was still impaired 350 days after irradiation.*

Previous reports (*1*) have presented data demonstrating in lethally x-irradiated (C57L × A)F₁ mice, protected with syngeneic bone marrow, that the ability to reject a first-set allogeneic skin graft recovers from the effects of x-irradiation prior to the ability to reject a first-set xenogeneic skin graft. The converse has been found to be true with respect to (C3H × DBA/2)F₁ mice (designated C3D/2 F₁), and the data supporting this are herein presented.

These data are interpreted as representing positive evidence for the existence within the mammalian "immune system" of two physiologically distinct "lines" of immunologically competent cells which possess dissimilar functional capabilities. That is, the xenogeneic skin grafts were rejected by a cell system not capable of rejecting allogeneic grafts and vice versa. These two cell systems manifest widely disparate rates of recovery from the effects of radiation.

Twelve- to 16-week-old male C3D/2 F₁ mice were used as skin graft recipients. Skin graft donors were adult male C3D/2 F₁ ($H2^k$-$H2^d$), A/HeJ ($H2^a$), BALB/c ($H2^d$), and C57L ($H2^b$) mice, and 3- to 4-week-old male and female Sprague-Dawley rats. The orthotopic tail skin grafting method of Bailey and Usoma was used (*2*). Mean survival time of the grafts and standard deviation are reported. The mice were protected against the lethal effects of the radiation by means of the intravenous injection of 4 to 6 × 10^6 nucleated syngeneic bone marrow cells and/or by means of urethan (1 mg/g, intraperitoneally), given daily for the 2 days prior to irradiation (*3*). The mice received 870 rad whole body x-radiation [250 kv (peak), 15 ma; HVL 1.5 mm Cu; 30 rad/min] and were grafted with C3D/2 F₁, A/HeJ, BALB/c, and rat skin 0.2, 62, 92, 240, or 350 days after irradiation. Several groups were regrafted after the first-set of grafts had been rejected; in addition, a skin graft

Table 1. Differential recovery of the first set response to allogeneic and xenogeneic skin grafts in lethally x-irradiated (870 rad) C3D/2 F_1 mice protected with urethan and/or syngeneic bone marrow.

Time grafted post-irradiation (day)	Treatment			Set	No. of mice	Mean graft survival time (days ± S.D.)			
	Urethan	Bone marrow	870 rad			A/HeJ	BALB/c	C57L	Rat
*				1	10	13.8 ± 1.6	14.4 ± 2.2		7.9 ± 0.6
*				2	9	6.1 ± 1.0	6.1 ± 1.4	9.2 ± 1.3†	3.0 ± 0.0
0.2	+		+	1	4	>140‡	>140‡		34.7 ± 3.0
0.2		+	+	1	6	81.8 ± 5.0	89.6 ± 10.0		28.0 ± 5.1
0.2	+	+	+	1	4	89.5 ± 5.0	89.5 ± 5.0		31.5 ± 2.4
62	+		+	1	4	>85‡	>85‡		12.5 ± 4.6
92	+		+	1	5	31.0 ± 13.3	40.0 ± 10.1		8.7 ± 0.6
92	+		+	2	4	6.3 ± 1.2	7.5 ± 1.1	11.7 ± 0.6†	4.0 ± 0.0
240		+	+	1	6	25.1 ± 9.1	30.0 ± 7.5		8.3 ± 1.3
240		+	+	2	6	17.0 ± 10.3	18.0 ± 7.2	22.0 ± 4.6†	
350		+	+	1	7	30.8 ± 3.1	33.4 ± 3.2		9.4 ± 0.4
350		+	+	2	7	12.3 ± 2.8	12.6 ± 2.7	15.4 ± 1.0†	4.3 ± 1.4

* First and second-set norms for nonirradiated adult male C3D/2 F_1 mice. † First-set C57L skin graft. ‡ The grafts were intact at the time the manuscript was prepared.

of a third H-2 type was placed (that is, first-set, C57L).

The mice grafted immediately after irradiation rejected their rat skin grafts in approximately 30 days but retained the allogeneic grafts over 80 days (several allogeneic skin grafts were intact at the time this report was written), regardless of whether they were urethan and/or bone marrow protected (Table 1). The first-set response to rat skin grafts was slightly impaired in the group grafted 62 days after irradiation but normal in the group grafted at 92 days. However, the first-set response to allogeneic grafts was still impaired in the group grafted 350 days after irradiation. The second-set response to allogeneic skin grafts was vigorous in the urethan-protected group grafted 92 days after irradiation but was grossly impaired in the bone-marrow-protected group grafted 240 and 350 days after irradiation.

These data clearly indicate that the cell system involved in the rejection of the xenogeneic (rat) skin graft is functionally distinct from that cell system involved in the rejection of the allogeneic skin grafts, being incapable of recognizing and/or reacting to the transplantation isoantigens of the allogeneic grafts. In addition, the data suggest that, in this strain of mouse, syngeneic bone marrow adds little, if anything, to the immunologic recovery of the lethally irradiated host (*4*).

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Renal Baroceptor Control of Renin Secretion

Abstract. *Small reductions in renal perfusion pressure to levels still within a physiologic range, which did not reduce renal blood flow, caused the kidney to release renin. Renin appeared in much larger amounts in renal-vein blood than in renal lymph. Release of renin appears to be mediated by a renal baroceptor rather than by ischemia.*

Sixty-five years ago the kidney was found to contain a substance that causes rise in arterial pressure when injected into a vein. It is still not known with certainty whether this substance, renin, may account for some forms of hypertension. The primary difficulty has been lack of adequate methods for its detection in circulating blood.

Renin is an enzyme; it raises arterial pressure by acting on alpha-2-globulin in blood to create a decapeptide termed angiotensin I. The two terminal amino acids of the decapeptide are split off by an angiotensin "activator"; the remaining octapeptide, angiotensin II, is a vasoconstrictor and the most powerful pressor substance known.

There is currently a revival of interest in the renin-angiotensin system as a cause of hypertension. This is due in large part to three recent developments: (i) the finding that human hypertension associated with partial obstruction of one renal artery is accompanied by increased amounts of renin-like activity in blood draining from that kidney (*1*), (ii) the development of techniques to visualize obstructive lesions of the renal arteries in hypertensive patients, leading to surgical repair and cure of the hypertension, and (iii) the discovery that angiotensin causes the adrenal gland to secrete aldosterone.

It has been assumed that if renin is released by the kidney it will pass directly into the renal-vein blood, but recently Lever and Peart (*2*) found renin in dog's renal lymph after partial constriction of a renal artery and in three experiments were unable to demonstrate it in renal-vein blood. This prompted us to examine the importance of this route of release compared to release directly into renal-vein blood (*3*).

In dogs, renal perfusion pressure was reduced by partially inflating a balloon that had been inserted into the aorta by way of a femoral artery and passed upward to just above the origin of the renal arteries. The left renal vein was cannulated by way of the left testicular or ovarian vein in order that renal-vein blood could be collected without obstruction of blood flow or interference with lymphatics. The thoracic duct, which drains renal lymph into the circulation, was cannulated in the neck, and a cannula was also placed in a peripheral artery. All samples of blood and lymph were heparinized and centrifuged for the same time at room temperature and the cell-free supernatants were frozen until the time of assay. Ten to 15 minutes elapsed between collection and refrigeration. Pressor material in plasma and lymph was assayed by intravenous injection of 0.1 to 0.4 ml into rats treated with a ganglion-blocking agent to enhance their pressor responsiveness.

Within 5 to 15 minutes after the balloons were inflated, there was, in all of nine experiments, a slow rise in