The greatest changes measured with our cell were approximately 3% of the total resistance. This value, of course, represents the much greater fall of the membrane resistance, shunted by the invariant low resistance of the fluid. Cole and Curtis obtained for the same measurement values as high as 7%, but their higher values can be ascribed to the smaller amount of shunting fluid in the measuring cells used by them. A few experiments using oil as the bathing medium gave much higher values. The resistance changes were largest for sea water and progressively smaller, but reversibly so, for the progressively Na^+ poorer solutions. On the other hand, there was a steady decrease of the amount of the measured resistance change with time.

The experiments reported here indicate that the membrane resistance change is a consequence of other events in the axonal membrane. They also constitute a further demonstration of the importance of the Na^+ component of the local circuit, first because the correlated temporal courses of the spike and of the resistance change are both functions of the external Na^+ concentration and, second, because of the magnitudes of both the spike and of the resistance change are also functions of the external Na^+ concentration. The latter correlation is of special importance to theoretical concepts of the processes involved in excitation and propagation.

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Blood Transfusion in Irradiation Hemorrhage[1]

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Among the postirradiation findings characteristic of near-lethal (LD_{50}–LD_{100}) exposures to ionizing radiation are spontaneous abnormal bleeding and anemia. Because of the prominence of thrombocytopenia and anemia in the abnormal bleeding syndrome of irradiation sickness, it is natural to assume that the frequent administration of fresh whole blood transfusions might be of considerable therapeutic value in the control or prevention of this type of hemorrhage. In spite of the logical nature of this anticipation, there are no experimental or clinical data to support the contention that blood transfusions will be of value in irradiation injury other than in the treatment of initial shock or in the prevention of anemia. Since no American doctor entered either Hiroshima or Nagasaki short of 4 weeks after the bombing, early laboratory data from these disasters are, for all practical purposes, nonexistent. In the absence of human data, our only recourse is to establish the pathologic picture and a therapeutic program based on observations carried out on the experimental animal.

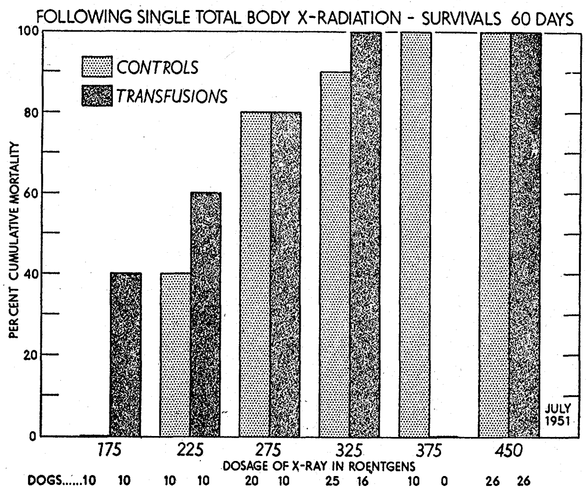

FIG. 1. Cumulative mortality in transfused and nontransfused dogs after exposure to x-radiation.

This is a study of the therapeutic value of blood transfusion given, without antibiotics, to determine whether this procedure will prevent irradiation hemorrhage and/or improve the survival rate in the x-irradiated dog. The dog was chosen because in many respects its response to total-body irradiation is similar to man. This animal differs in one important respect in that its blood types are much less well defined. As seen below, the results obtained from transfusion alone are the reverse of those anticipated.

One hundred and seventy-three dogs were exposed to single doses of total-body x-irradiation at the following dosage levels: 175, 225, 275, 325, 375, and 450 r. The animals were divided into two groups; one group of 101 dogs served as controls, and the other group of 72 was transfused with citrated fresh whole blood 3 times a week beginning on the fourth postirradiation day. Five ml/kg of body weight was administered on each day the animal was transfused. In addition to this blood the animal also received a volume of blood equivalent to the amount withdrawn for study just prior to each transfusion. No other treatment was administered.

For comparative purposes the experiment was so arranged that animals receiving blood were paired with control animals of approximately the same size, which were irradiated under similar conditions on the same day. All were mongrels, and both male and female dogs were used.

Total-body exposures were administered, placing the unanesthetized dog in a canvas sling suspended before the energy source, a GE Maximar 250-kv,

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TABLE 1

AVERAGE POSTIRRADIATION LIFE OF THE NONSURVIVALS

	450 r	375 r	325 r	275 r	225 r	175 r
Controls	10.4 days	13.3 days	11.7 days	16.4 days	17.2 days	All survived
Transfusions	9.7 "	None studied	11.8 "	17.8 "	18.1 "	22.5 days

15-ma x-ray machine. A combination 1-mm copper and 3-mm bakelite filter was used. The target distance was 57 in. to the projected center of the animal, and the average rate of delivery was 5.12 r/min. To achieve a given dosage level, exposure time was adjusted accordingly. All other physical factors were constant. In each instance one half the total dose was delivered from one side, then the animal was rotated 180° within its sling and the exposure was completed.

The following studies were conducted for both control and transfused animals: (1) the whole blood clotting time; (2) the Quick one-step prothrombin time; (3) the erythrocyte, leucocyte, and thrombocyte counts, and hemoglobin determinations; (4) weight records 3 times/week; and (5) daily rectal temperatures.

All bloods were cross-matched prior to transfusion. Autopsies were performed on 95% of the transfused dogs and on 91% of the controls. The incidence and site of hemorrhage at autopsy were classified according to the organs and tissues in which bleeding occurred.

Fig. 1 demonstrates that citrated whole blood transfusions, alone and under these conditions, did not increase survival over that of the controls. Table 1 shows the average postirradiation life of the nonsurvivals of controls and transfused animals at the exposure levels used.

TABLE 2

LOCATION AND FREQUENCY OF GROSS HEMORRHAGE IN CERTAIN AREAS IN X-IRRADIATED DOGS

Location of hemorrhage	Frequency in 69 control dogs*	Frequency in 53 transfused dogs†
	(%)	(%)
Skin (other than venepuncture sites)	28	21
Gingiva	50	38
Chest		
Parietal pleura	69	66
Mediastinum	43	48
Lungs		
Hilar hemorrhage	49	46
Pneumonia	82	88
Heart		
Pericardium	53	58
Epicardium	66	73
Diaphragm	27	23
Abdomen		
Retroperitoneal	26	34
Stomach	52	46
Intestine	77	67
Colon	61	51
Kidneys	25	37
Bladder	32	34

* Sixty-nine autopsies done, 10 not done, 22 survivors.
† Fifty-three autopsies done, 7 not done, 12 survivors.

Table 2 indicates that gross hemorrhages found in certain organs and tissues at autopsy were as frequent in the transfused irradiated dogs as in the untreated controls. Sixteen other hemorrhagic sites, showing similar data, are excluded from Table 2 in the interest of brevity.

No significant or consistent drop in prothrombin activity in either the transfused animals or their controls was apparent, and, as illustrated in Fig. 2, transfusion alone failed to prevent or control the postirradiation increase in the whole blood clotting time.

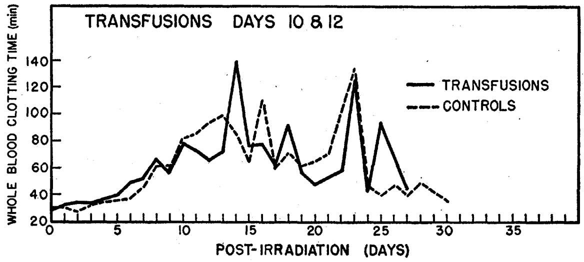

FIG. 2. Average whole blood clotting time in transfused and control dogs following radiation.

Fig. 3 shows the failure of blood transfusion to prevent or correct postirradiation thrombocytopenia or leucopenia. The only benefit observed in blood transfusion was that it prevented the full extent of irradiation anemia (Fig. 4).

There was no consistent difference between the two groups in febrile response or in weight loss characteristic of postirradiation sickness.

These data indicate that blood transfusion without

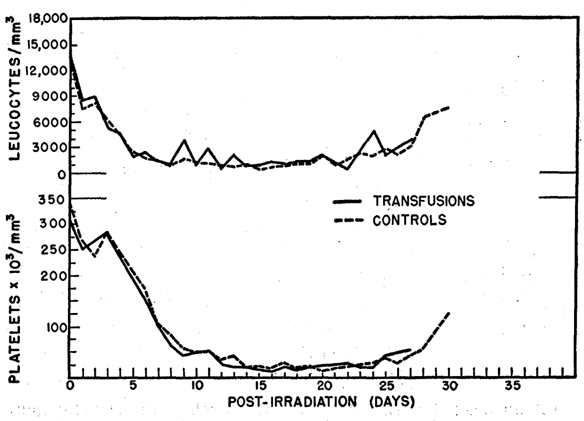

FIG. 3. Average platelet and leucocyte counts of transfused and control dogs following radiation.

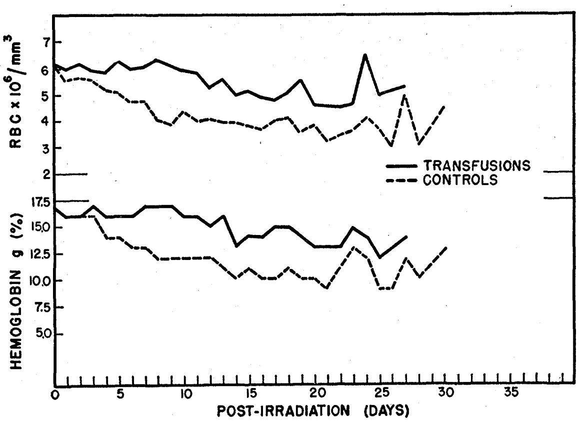

FIG. 4. Average erythrocyte count and hemoglobin of transfused and control dogs following radiation.

antibiotics under the experimental conditions described here is of no benefit either in preventing or in treating irradiation hemorrhage, in lessening the changes in coagulation for untreated animals, or in improving survival rate or time. In some animals the bleeding actually increased in severity after transfusion, and this was accompanied by a further increase in the whole blood clotting time. Moreover, if the numbers of animals can be considered sufficient to decide the influence of transfusion upon survival rate and time, it can only be concluded that transfusion was deleterious.

Some of the animals displayed symptoms of transfusion reactions, as reported previously (*1*). It is possible that others also had mild reactions that were not clinically detectable. Transfusion reactions in the nonirradiated dog are remarkably rare, whereas after irradiation they occur with sufficient frequency to present a definite risk. The reactions noted were anaphylactoid in nature. Alterations in the clotting time and in the protamine titration, when they resulted from the transfusion reaction, were overcome by the administration of protamine sulfate or toluidine blue (*1*). Bleeding from ulcerated areas, the continued formation of petechiae, and the hemorrhagic gastroenteritis, however, were not influenced by these agents.

Endogenous heparinemia is characteristic of anaphylactoid reactions (*2*) and may be associated with blood transfusions which also are anaphylactoid in character. The recent reports of Muirhead (*3*) and of Friesen, Harsha, and McCroskey (*4*) are of great interest. These two groups reported that the abnormal bleeding during or following surgery often was the result of minor or major incompatibility of transfused blood. In each instance where this was recognized prompt cessation of bleeding was associated with the administration of toluidine blue or protamine sulfate. We have repeatedly observed and reported the same findings.

The University of Kansas group was also able to reproduce the type of bleeding described above by the repeated transfusion of blood in pure-bred Boxer dogs (*4*). In 4 of 6 animals so afflicted, death resulted from spontaneous hemorrhage before antiheparins could be given.

If man, like the dog, is more susceptible to transfusion reactions following irradiation injury, when he already is bleeding from thrombocytopenia, capillary injury, and ulcerative alimentary lesions, the administration of whole blood transfusion should not be attempted unless protamine sulfate or toluidine blue is available in case transfusion reactions occur and increase the bleeding tendency.

The one beneficial effect of blood transfusion that is brought out by these experiments is the correction of anemia, provided sufficient quantities of blood are administered. If these data can be applied to man under similar circumstances, 300–500 ml of blood, given 3 times per week starting on the fourth day, should be sufficient to maintain the erythrocyte count above 3,500,000/cm^3 and hemoglobin concentrations above 10 g%. It is clearly apparent, however, that the postirradiation anemia in the dogs is of little, if any, consequence in determining their fate or rate of survival. Our observations should not discourage the use of blood with other therapy in irradiation injury, since our animals died before they developed a profound anemia, and these data in no way question the need of blood transfusion in the treatment of anemic anoxia.

The data herein presented do not take into account the possibility that blood transfusion combined with antibiotic and/or other therapy may prove beneficial. In a previous report (*1*) it was observed that blood transfusion combined with daily administration of aureomycin enabled 2 of 11 dogs to survive a 450 r total-body x-radiation, whereas 14 similarly irradiated dogs receiving only aureomycin, on the same schedule, died. Animals receiving blood transfusion together with aureomycin fared better than those receiving aureomycin alone. Irradiation hemorrhage was not noticeably reduced in either case. Considerably more data are necessary, however, before the effect of blood transfusions combined with antibiotic therapy can be evaluated. Studies of this nature that are currently under way appear more hopeful.

These experiments clearly indicate that the frequent transfusion of blood without antibiotics is futile in the treatment or prevention of irradiation hemorrhage in dogs and that it gives no evidence of increasing survival rate or time. It does not follow that man, similarly exposed to ionizing irradiation, would not benefit from frequent transfusion, because the status of blood types and transfusions in dogs is ill defined and may not be appropriate for human comparison. On the other hand, it could prove disastrous to depend on blood transfusion to control irradiation hemorrhage in man, should the response in the irradiated human patient to blood transfusion be similar to that in dogs. Further experience with transfusions given dogs and other species, especially some of the subhuman primates, is urgently needed. If blood transfusion appears to offer little hope in controlling irradiation hemorrhage in man, this knowledge would afford a more intelligent basis for the use of blood and would channel the limited supply available in the directions in which it may be used most effectively.

The frequent administration of fresh blood transfusions without antibiotics in dogs failed to improve the survival rate or to ameliorate spontaneous bleeding after exposures to total body x-radiation (LD_{50}–LD_{100}). On the basis of these experiments a more cautious attitude toward the use of frequent blood transfusion alone as a therapeutic measure in the treatment of the *latent* symptoms of irradiation injury in man may be indicated. These data do not relate in any manner to the use of blood in the treatment of shock incident to the *early* blast effects of an atomic burst, or to blood needs in anoxic anemia, where the therapeutic importance of adequate blood and plasma transfusion is soundly established.

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Comments and Communications

Some Punkins!

DR. ZACKS' statistical note on "How Does the Ivy Grow?" in SCIENCE (**114**, 332 [1951]), with a later correction (**114**, 469 [1951]), is interesting, but either Harvard ivy is a laggard as regards its rate of growth, or else the fertility of Boston soil falls far short of that in the garden of a member of the University of Missouri faculty, as these records will show.

A single stray pie-pumpkin seed was found sprouting in a row of garden beets on May 17, 1951, and the plant was permitted to "root for itself" until killing frosts laid it low while still in the vigor of life on November 5, 1951. The plant received no added fertilizer and no cultivation or other care, except that some of the more ambitious runners were turned back into the garden from a traveled city alley at the edge of the garden. In all fairness, however, it should be said that there were no squash bugs in the garden to pester it.

In the 173 days, or 249,120 minutes, of its active life the plant produced a total over-all vine growth of 1986 ft, or 605,332.8 mm. This would mean a total average vine growth of 2.43 mm/min. However, this is a measure of total vine growth and not of the tip growth of any one runner. The longest single branch measured slightly over 75 ft, or 22,860 mm, which means that this vine made an average tip growth throughout the summer, rain or shine, of .092 mm/min. Observations showed that at the peak of growth it was greatly exceeding this record. In other words, this vine made an average daily growth of over 5 in., so one could actually see it grow.

But that is not all. While growing almost twice as fast as the ivy, this vine also produced 20 pumpkins weighing a total of 300 pounds, besides several small immature ones. In kitchen parlance this means that the vine produced one pumpkin pie every 7 hr. It overran every growing thing, including a grape arbor, fruit trees, and flowers, in 1600 square feet of garden space. Some of its leaves were 15 in. across. And yet the whole story of this waif of a pumpkin seed has not been told, for during its remarkable vegetative growth and its production of the makings of over 500 pies, the seed actually reproduced itself twenty thousandfold, for the 20 mature pumpkins contained an average of 1000 seeds each. To my way of thinking, the Harvard ivy, with no serious accomplishments to its credit other than tip growth and perhaps a few seeds, really made a poor showing.

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The Alleged Disappearance of Hunger During Starvation

KEYS *et al.* (*1*) stated that the sensation of hunger disappears in a matter of days during total starvation, but that no diminution of hunger occurred during a type of semistarvation studied by them. Cannon (*2, 3*) seems to have been mainly responsible for the persistence of claims that hunger sensations cease after the first few days of starvation, although he made no study of hunger during prolonged starvation. Cannon only cited reports made by others, including hunger-strikers and individuals who tried the fasting cure (*4*). One of us (F. H.), after having fasted 8 days in 1912 and 26 days in 1913, also believed that the reference of hunger to the stomach disappeared in 5 or 6 days. In 1916, he thought that the senior author's study during 5 days of starvation (*5, 6*) was not sufficiently prolonged to reveal the true nature of hunger. Hence, a study of hunger was made by the senior author in which the junior author served as the subject during a 15-day fast in 1917 (*7*).

It was found that the periodic gastric contractions, which Cannon as well as the senior author attributed to hunger, persisted throughout the 15 days of fasting, and that the desire to eat or to resume eating was always keenest when the periodic gastric contractions occurred. A modification of the sensations was experi-