only in the presence of plasma from tuberculous subjects. White blood cells from healthy tuberculin-negative humans will undergo similar tuberculin cytolysis in the presence of such tuberculous plasma.

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The Role of the Spleen in Radiation Injury.*

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Ectopic blood formation in the spleens of mice injected with a dose of 2.0 microcuries per gram of body weight of radiostrontium (Sr^{89}), as shown by Jacobson *et al.*,[1,2] was sufficient to obviate the development of anemia even though the bone marrow was largely destroyed and only gradually reconstituted over a period in excess of 100 days. Splenectomized mice given this dose developed a severe anemia, recovery from which occurred only as the hematopoietic activity of the bone marrow recovered. This communication describes a somewhat different but related technic for studying the significance of the spleen in recovery from or compensation for radiation injury.

Materials and Methods. Four groups of young female mice were prepared as indicated in Table I. Mice in Group I were untreated controls. The mice in Groups II, III, and IV were anesthetized, an incision made in the left upper quadrant of the abdomen, and the spleen brought out through the abdominal incision with the main pedicle intact. Group III and Group IV mice were irradiated with 600 r whole-body X radiation (250 Kv) except that during the irradiation the mobilized spleens of Group IV mice were placed in one-quarter inch thick lead boxes with openings for the pedicle only. The mobilized spleens of Group III mice were placed in thin paraffin boxes which offered no appreciable shielding from the radiation. The mobilized spleens of Group II mice (operated controls) were placed in lead boxes for a period equal to the time that Group III and Group IV spleens were thus contained. The radiation required approximately 12 minutes after which the spleens of groups II, III, and IV mice were returned to the abdominal cavity and the operative incisions sutured.

Results. Hematologic studies were made on all 4 groups. Animals from each group were sacrificed at intervals for histopathologic study.

The mean hemoglobin, erythrocyte, and hematocrit values of Group IV (lead-protected spleens) were not significantly altered when compared to control Groups I and II (Fig.

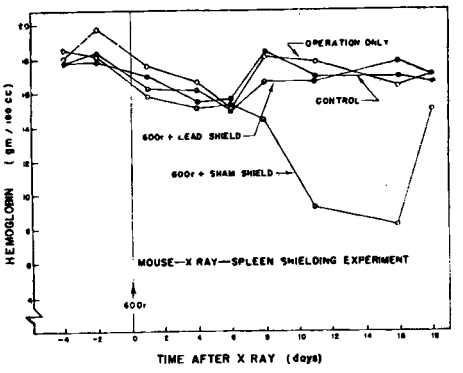

FIG. 1.
The hemoglobin values of control mice and mice exposed to 600 r with and without lead protection of the spleen.

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1 Jacobson, L. O., and Simmons, E. L., *Anat. Rec.*, 1948, **100**, abstract.

2 Jacobson, L. O., Simmons, E. L., and Block, M. H., National Nuclear Energy Series, Div. IV, Vol. 22B.

TABLE I.
Preparation and Treatment of Animals.

Group	No. of animals	Preparation of animals	Treatment
I	15	None	None
II	20	Anesthetic (Nembutal) Surgical mobilization of spleen	"
III	20	Anesthetic (Nembutal) Surgical mobilization of spleen	600 r total body X irradiation inclusive of spleen
IV	20	Anesthetic (Nembutal) Surgical mobilization of spleen	600 r total body X irradiation exclusive of spleen

1-3). In Group III (spleens unprotected), however, these values were markedly reduced between the sixth and eighteenth day after irradiation. The mean reticulocyte value of Group III animals (spleens unprotected) was reduced to less than 0.1% by 2 days and remained reduced through nine days (Fig. 4). The mean reticulocyte value of Group IV mice (lead-protected spleens) was not significantly reduced at any time; a definite increase above the normal value occurred between the third and fourteenth day. The mean platelet value of Group III (spleens unprotected) fell gradually to a minimum of 15,000 cu mm on the eighth day and rose to a normal value by the eighteenth day after irradiation, whereas the platelet value of Group IV (lead-protected spleens) reached a minimum of 230,000 cu mm on the ninth day and rose to a normal value by the eleventh day. (Fig. 5) The mean leucocyte value of Group III (spleens unpro-

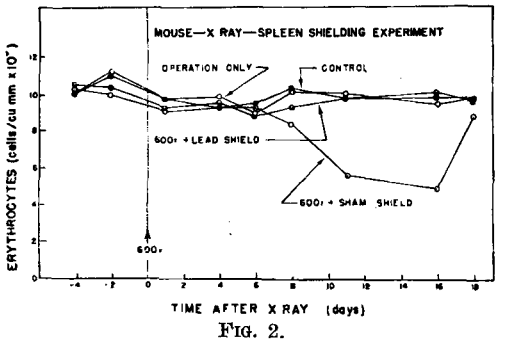

FIG. 2.

The erythrocyte values of control mice and mice exposed to 600 r with and without lead protection of the spleen.

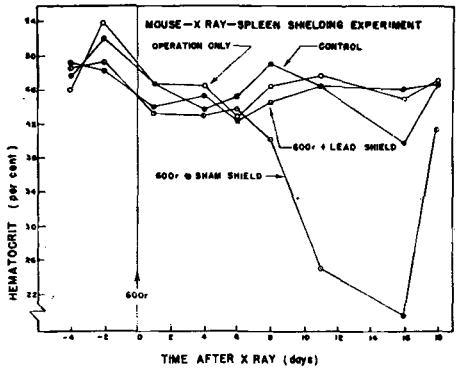

FIG. 3.

The hematocrit values of control mice and mice exposed to 600 r with and without lead protection of the spleen.

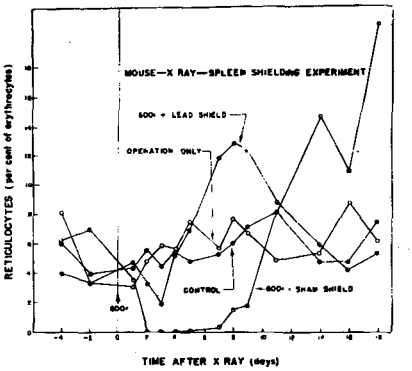

FIG. 4.

The reticulocyte values of control mice and mice exposed to 600 r with and without lead protection of the spleen.

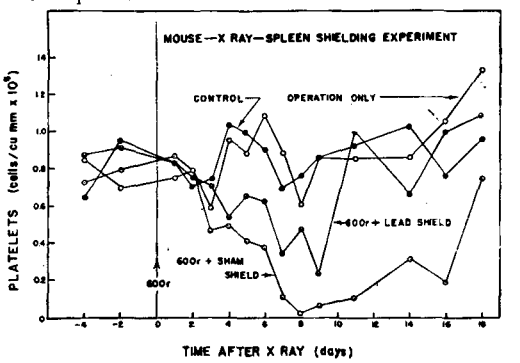

FIG. 5.

The platelet values of control mice and mice exposed to 600 r with and without lead protection of the spleen.

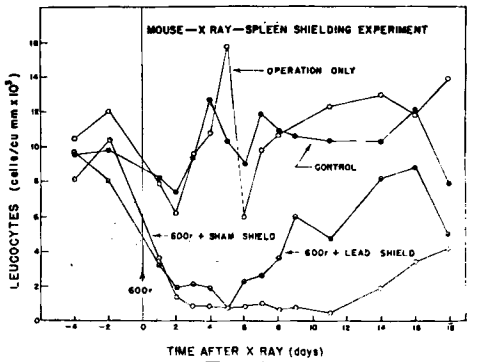

FIG. 6.

The leucocyte values of control mice and mice exposed to 600 r with and without lead protection of the spleen.

tected) was reduced below 1000 per cu mm by the third day and remained below 1000 through the eleventh day after irradiation. The mean leucocyte value of Group IV (lead-protected spleens) fell to a minimum of circa 2000 per cu mm only and rose to a relatively normal value by the ninth day after irradiation (Fig. 6).

The spleens of Group III (spleens unprotected) decreased markedly in size within twenty-four hours and remained thus reduced in size beyond the tenth day after irradiation. The spleens of Group IV (lead-protected spleens) increased in size reaching in some instances approximately twice the size of controls by the third day.

The histologic studies revealed that hematopoietic tissue in Group III animals that received 600 r inclusive of the spleen was largely destroyed with significant regeneration only beginning after the sixth day. A comparable degree of destruction of hematopoietic tissue occurred in Group IV animals except in the lead-protected spleens where a marked increase in erythrocytopoiesis, megakaryocytopoiesis, and granulocytopoiesis was already apparent by 18 hours after exposure. This ectopic blood formation in the spleen increased rapidly in extent. Lymphatic tissue in these lead-protected spleens decreased however, as the erythro-, granulo-, and megakaryocytopoiesis increased. By forty-eight hours after irradiation the amount of lymphatic tissue remaining in the lead-protected spleens was approximately 75% less than controls and consisted largely of medium and small lymphocytes about the arterioles in the white pulp.

Summary and conclusions. These hematologic and histologic data indicate that:

1) Severe anemia, leucopenia, and thrombocytopenia develop in mice after a single dose of 600 r whole-body X radiation.

2) Ectopic erythrocytopoiesis, in the lead-protected spleens of mice given 600 r whole-body X radiation (exclusive of spleens) compensates with such rapidity and so extensively for the destruction and interruption of this activity in the marrow spaces that no anemia of significance becomes apparent. Ectopic granulocytopoiesis and megakaryocytopoiesis in the lead-protected spleens compensates significantly but at a slower pace and less completely for the bone marrow destruction.

3) A marked and sustained decrease in the amount of lymphatic tissue is produced in the lead-protected spleens of animals given 600 r whole-body X radiation. This decrease in lymphatic tissue may perhaps be a result of (a) unsuccessful competition of the lymphatic tissue with the ectopic hematopoiesis for nutritional requirements, (b) actual indirect effect of radiation and (c) a differential humoral suppression from some unknown site.

The rapidity with which erythrocytopoiesis transfers from the X-ray damaged bone marrow to the lead-protected spleen in the absence of anemia suggests that the mechanism of stimulation of erythrocytopoiesis under the conditions of this experiment may involve some factor or factors other than, or in addition to, the accepted hemoglobin-oxygen relationship.

This technic permits more or less exclusive protection of the spleen or the appendix or other visceral tissues from irradiation while applying various dosages to the remainder of the body. It provides a method of studying potential sites and mechanism of the production of ectopic blood formation, possible secondary effects of radiation as well as offering possibilities for determining the potential role of such sites in immune reactions, in preventing or alleviating radiation-induced hemorrhagic phenomena and in the study of survival or recovery from radiation injury.