material. This procedure resulted in a permanent suppression of marrow. From 11 to 41% of the total marrow was obliterated by this method. The effects on cell and hemoglobin content of peripheral blood were investigated. In most of the animals there were no significant permanent changes. Extirpation of the marrow was followed frequently by an increase in leukocytes and a decrease in hemoglobin, erythrocytes and platelets. When more than 6 marrows were ablated, some of the animals developed a slight reduction in all the elements investigated. An infrequent animal showed significant changes. Leukocytes were increased in number and the peripheral blood was suggestive of leukemia. Appearance of immature granulocytes and a high leukocyte count was associated with a reduction of hemoglobin and erythrocytes and morphologic abnormalities of red blood cells.

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Tissue Changes in Rabbits with Ablation of Marrow of Long Bones.

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In previous articles a method of replacing marrow of long bones with inert material was described.[1,2] The procedure reduces the marrow content of the body of the rabbit by approximately 41 ± 5%.[3] In this paper tissue changes incident to the substitution of marrow by inert material are described. Thirty rabbits were used in this experiment over a period of 3 years. Some of the animals died and others were killed in from 10 days to 14 months after removal of the marrow. In the 30 rabbits, 11 to 41% of the marrow was ablated in from 4 days to 5 months. Gross and histologic observations were made of all the thoracic and abdominal viscera, the remaining marrow and occasionally of the pituitary gland.

In 6 animals 41 ± 5% of the total marrow was replaced by inert material over a period of 2 to 5 months and the animals were allowed to survive for total periods of 4 to 14 months. Of the 6 animals, 4 showed infiltration by mature and immature granulocytic leukocytes of liver, kidneys, spleen and in 2 instances of the heart muscle and lungs. One animal showed a slight degree of infiltration of liver and kidneys and in the sixth there were no infiltrative changes (Fig. 1).

In 14 animals, 37 ± 5% of the marrow was ablated. The animals were allowed to survive from 2 to 14 months. Nine of the rabbits developed cell infiltration of liver, kidneys, spleen and in some there was involvement of the adrenals. Four rabbits showed a slight infiltration of liver and spleen only. One animal did not have any infiltrative changes.

In 7 rabbits 29 to 37% of the marrow was replaced by inert material. The total survival period of each animal did not exceed 2 months. Very slight cell infiltration was found in one animal. There were no infiltrative changes in the others.

In 3 animals from 11.5 to 23% of the bone marrow was removed and the total survival period varied from 1 to 4 months. There was no cell infiltration in any of the organs (Table I).

The unextirpated marrow from ribs, ulna and radius was correlated with the infiltrative changes in the other organs. The radius and ulna in an adult rabbit are acellular and were used as a criterion for the demand

1 Steinberg, B., and Martin, R. A., PROC. SOC. EXP. BIOL. AND MED., 1946, **61**, 428.

2 Steinberg, B., and Martin, R. A., PROC. SOC. EXP. BIOL. AND MED., 1946, **63**, ...

3 Dietz, A., PROC. SOC. EXP. BIOL. AND MED., 1944, **57**, 60.

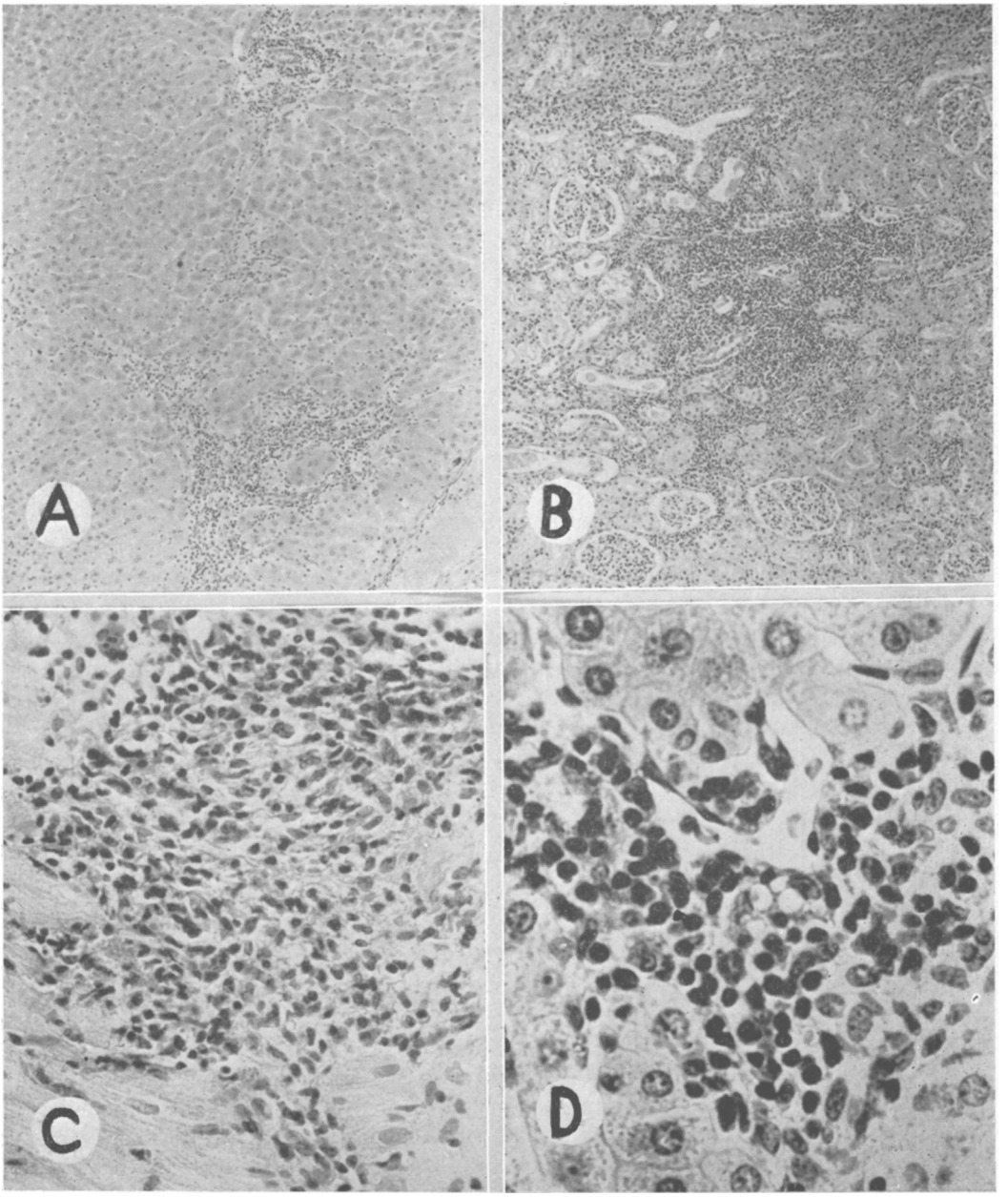

FIG. 1.
Infiltration of organs by mature and immature granulocytes after extirpation of marrow of long bones. A. Liver with patchy cell infiltration. B. Kidney with a patch of cell infiltration. C. Heart muscle with patchy cell infiltration. D. Higher magnification of cell infiltrate of liver.

of cells by the organism. The rib marrow is normally cellular with a fairly constant proportion of cell types. This marrow served as indicator of change in cell type. Cellular infiltration of the viscera, usually, coincided with the degree of cell hyperplasia in the remaining marrow. However, in some of the rabbits hyperplasia of the marrow was not

TABLE I.
Effect on Tissue After Permanent Ablation of Bone Marrow in Living Rabbits.

No. of rabbits	% of marrow replaced by inert material	Total duration of exper.	No. of animals with degree of cellular infiltration of organs	Organs involved by cell infiltration	Cellularity of usually inactive marrow	Size of adrenals in mg	Max. peripheral leukocyte count per cu mm of blood
			2 +++	liver, kidneys, spleen, heart and lung.		400 750 850	10,800
6	41 ± 5	2 to 14 mo.	2 ++	liver, kidneys and spleen.	3 very cellular 2 slightly 1 acellular	950 1070	to 19,600
			1 ± 1 neg.	kidneys and spleen.		1075	
			3 +++	liver, kidneys, heart, spleen and lymph nodes		2-300 or less	12,300
14	37 ± 5	2 to 14 mo.	6 ++	liver, kidneys and spleen	9 very cellular 4 slightly 1 acellular	4-860 or less 8-1850 or less	to 49,800
			4 +	liver and either spleen or lymph nodes.			
			1 neg.				
7	29 to 37 ± 5	10 da. to 2 mo.	1 +	liver, lungs and spleen.	very cellular with increase of immature forms	850 to 1075	16,000 to 135,300
			6 neg.				
	11.5	2 mo.	,,	neg.	moderately to very cellular	275	18,000
3	16	1 ,,	,,	,,		315	17,950
	23	4 ,,	,,	,,		350	30,800

neg. No cell infiltration.
± Questionable infiltration.
+ Very slight infiltration.
++ Slight to moderate infiltration.
+++ Moderate infiltration involving more than 2 organs.

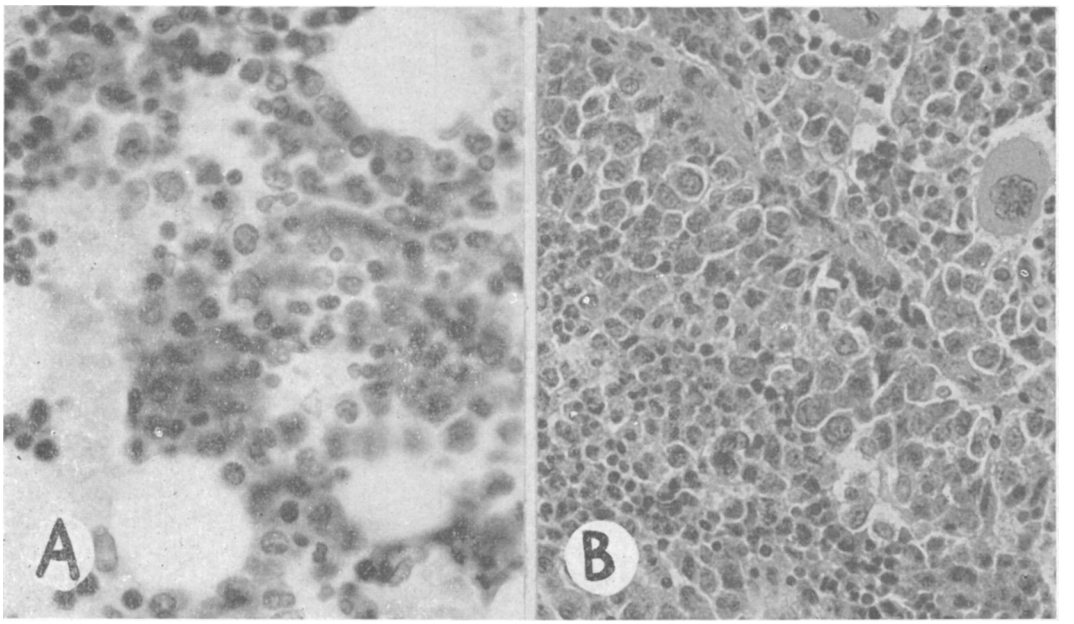

FIG. 2.
Effect of replacement of marrow of long bones with inert material on remaining marrow. A. Marrow of radius. In normal adult rabbits this marrow is aplastic. In this instance the marrow is hyperplastic and contains mostly immature cells. B. Rib marrow. There is considerable increase in cellularity with a change to a predominantly immature type of cell.

associated with infiltration in other organs. In 2 instances with organ infiltration, the marrow of radius and ulna was aplastic and only moderately cellular in the ribs. (Fig. 2).

The adrenal gland in most instances of marrow extirpation became increased in size. The increase was due to hyperplasia of the cortical cells and largely of the zona fasciculata. The average weight of both adrenals in 25 normal rabbits was 260 mg. Observation of adrenal weight in many other normal rabbits disclosed an occasional large pair adrenals with maximum weights of 700 to 1275 mg. Neither the age nor the weight of the animal affected significantly the weight of the adrenals. In animals with more than 16% extirpated marrow the average weight of adrenals was 867 mg. In many individual animals the weight of the glands exceeded 1000 mg. (Table I).

Summary. From 11.5 to 41 ± 5% of the total bone marrow was extirpated in 30 rabbits and the bone cavities were filled with inert material. The animals were allowed to survive for periods of 10 days to 14 months. Tissue changes were correlated with the quantity of marrow removed and the duration of survival of the animal. In some of the organs there appeared a cell infiltration of mature and immature granulocytes similar to that seen in human aleukemic leukemia. The marrow of the radius and ulna, normally aplastic for an adult rabbit, and the rib marrow showed marked cellularity in most animals. There was a considerable number of immature granulocytes in the marrow of some rabbits. The adrenal glands were increased in weight due to hyperplasia of the zona fasciculata.