enteritidis and normal ones (Tables II and III).

Finally, mice starved from 1 to 8 days were tested for retention of the dye (Table IV). It is of interest that a mild increase in the retention of bromsulphalein arose even in the early days of starvation. Beginning with the 5th day, however, at a time when either marked fatty infiltration or necrotic lesions was observed histologically and mice had begun to die, the retention of bromsulphalein was decidedly increased, as shown by the fact that all but 2 of the mice tested on the 5th day or later had readings higher than 1 mg.

Summary. Six tests for the study of hepatic dysfunction and damage were applied to Swiss mice. Insufficiently sensitive to detect hepatic lesions were the thymol-turbidity test, plasma-coagulation time and vaginal-smear cytology. Cephalin-cholesterol flocculation was not applicable owing to the fact that normal mouse sera reacted positively. Blood-bilirubin determinations indicated hepatic lesions induced by carbon tetrachloride or phosphorus. The increase in bilirubin in the blood, however, even in cases of extensive damage, was not high; 0.3 mg per 100 cc of plasma in control mice as an average, as compared with 0.6 mg per 100 cc in those with carbon tetrachloride lesions.

Retention of bromsulphalein was the most useful and accurate of all the tests described herein. A base line was established for control mice; *i.e.*, less than 1 mg of dye retained per 100 cc of plasma could be regarded as normal. In mice with hepatic lesions, tested at a proper time and within the limitations mentioned, values 10 or 20 times higher than the normal were not unusual. Since retention of this dye was increased by diverse methods such as chemical poisoning, bacterial infection, starvation, and injection of autolyzed tissue, its use may be of value in the study of experimental problems connected with hepatic injury of mice.

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Permanent Ablation of Bone Marrow in Long Bones of Living Rabbits.

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In a previous paper a method of removing marrow from a single bone in living rabbits was described.[1] In this article a procedure is outlined in which the marrow of all the long bones was removed and replaced by inert material. The regeneration of marrow was prevented permanently in the bones so treated. On the basis of Dietz's analyses of distribution of bone marrow,[2] it was estimated that approximately 41 ± 5% of the total marrow may be ablated by this method.

The rabbit was the animal of choice. The marrow in this animal is tubular and with very few connective tissue bands which bind it to the endosteum. The complete marrow is therefore readily expressed. The animal is also sufficiently large to withstand several operative procedures. The marrow was removed from 2 to 10 bones: both tibiae, both femora, both humeri, and both radii and ulnae. The marrow of all other bones is inaccessible by this method. Thirty rabbits were used in the experiment over a period of 3 years.

The animals were anesthetized with pentobarbital sodium. The initial steps in drilling holes in the bone with a Ralk nail drill and expressing the marrow were similar to those already described.[1] Cotton strips of varying lengths and thickness were saturated in bone wax and autoclaved in Petri dishes. The

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

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

strips of cotton were introduced into the marrow cavity with a thin bladed thumb forceps and forced down with a blunt, fairly flexible probe. Both epiphyseal ends were plugged first with soft bone wax which was followed with wax-saturated cotton. Pressure by the harder cotton occasionally produced shock and death of the animals. The entire marrow cavity was packed tightly. This method of packing resulted in the expulsion of remaining bits of marrow and prevented regeneration of marrow in loosely filled places. Many other procedures in filling the marrow cavity were tried such as filling with a paste by means of needle and syringe. The method described, although more time consuming and laborious, was found to conform to the requirements of the experiment.

In 24 animals, the marrow of 1 to 3 bones was replaced with inert material at a single operation at intervals of 2 to 4 weeks. In 6 animals, the marrow of all the long bones on one side of the body, tibia, femur, humerus, radius and ulna, was replaced at one operation. The marrow of all the long bones of the other side was removed from 5 to 7 days later. These varying time intervals allowed to study the effects of rapid and gradual ablation of bone marrow.

The marrow cavities and the bones were examined at intervals over a period of 3 years. There was an initial thickening of the bone in the first several weeks followed by a slight degree of reduction in thickness. Whenever the packing was not complete, proliferating endosteum and marrow were found formed between bone and packing.

Summary. A method of ablating permanently the marrow of all the long bones in living rabbits is presented. The ablation may be carried out rapidly over a period of a week or gradually over several weeks. Approximately 41 ± 5% of the total marrow of the animal may be ablated permanently by this method.

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Effects of Permanent Mechanical Ablation of Marrow of Long Bones on Peripheral Blood of Living Rabbits.

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We described in previous articles procedures of removing marrow from long bones of living rabbits and replacing it with an inert material.[1,2] The total marrow of the body may be reduced by 41 ± 5% by this method.[3] Thirty rabbits were used over a period of 3 years in this experiment. In 24 animals the marrow was removed gradually over a period of 22 days to 5 months. In 6 rabbits the marrow was replaced within one week. The 30 animals were observed for periods of 10 days to 14 months after ablation of the marrow. Marrow was removed from 2 to 10 of the long bones with a reduction of 11 to 41% of the marrow. The marrow of the radius and/or ulna on one side was left frequently intact. The marrow of these bones is completely inactive in mature animals. Peripheral erythrocyte, platelet and leukocyte counts, hemoglobin determinations and studies of stained blood smears were made at frequent intervals before and after removal of marrow.

After removal of marrow there was an initial rise in the number of peripheral leukocytes in most of the animals. In some of the rabbits there was a drop. The change in the peripheral content of the cells re-

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.