crease in P^{32} and a very small decrease in Ca^{45} specific activities.

Summary. The effect of parathyroid extract administration upon the removal of radiocalcium and radiophosphorus from the long bones of sheep and its subsequent excretion in the urine was studied. Over a 5-day period of treatment, radiophosphorus but not radiocalcium was removed from the bone. The parathyroid extract produced only a slight rise in the urinary excretion which may be accounted for by the elevated serum phosphorus. Daily doses of 1000 i.u. of parathyroid extract over a 7-day period resulted in elevation of the serum phosphorus levels but not of serum calcium. It is concluded that in the sheep, parathyroid extract acted directly upon the bone and that any effect upon the kidney was minor in the dosage range and time periods employed; also, it appeared that phosphorus metabolism was much more influenced than was calcium metabolism.

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Prolonged Administration of Chloramphenicol in Monkeys. (20859)

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The relationship of chloramphenicol to blood dyscrasias in certain susceptible persons has been reviewed recently(1). To date no standard method is available to predict by experimental methods the potential hemocytotoxic effects in humans of new drugs. In earlier studies from this laboratory, the monkey has proved to be a valuable animal for hematologic study(2-5). It is the purpose of this paper to present the results of prolonged chloromycetin administration to monkeys.

Methods and materials. A total of 15 young adult *Macaca mulatta* were used in these preliminary studies. One group of 6 animals was administered 750 mg of chloromycetin daily except Sundays for 15 months from July, 1952 through October, 1953. The contents of 3 250 mg capsules were suspended in water, drawn up into a 50 ml syringe and introduced by stomach tube. Any residual material was rinsed through with water. Since these animals weighed between 5 to 6 lb at the beginning, the dosage approximated 250-350 mg/kilo. Two monkeys received a similar daily dose on alternate weeks for 15 months. Two had daily doses of 5 g and another 2 received 470 mg chloromycetin palmitate twice daily. Another pair of monkeys were started on 750 mg daily after receiving 200 r of total body irradiation. Three monkeys, after 2 months on vit. B-free synthetic diet, were given 750 mg chloromycetin daily along with a normal diet. Five to 7 complete blood counts were performed over a 2-week period before therapy, for base-line purposes. In addition, a pre-treatment bone marrow aspiration was also done. Serial blood counts (total 90 to 100) were then done daily during the first month and then bi-weekly thereafter. Bone marrow aspirations (total 6 to 7) were performed at approximately 2 to 3 month intervals. Chemical(6) and microbiologic(7) determinations of chloromycetin were done at weekly intervals to insure absorption of the drug. Weights were checked weekly.

Results. As can be seen in Fig. 1, 6 monkeys (A,B,C,D,E,F) given 750 mg daily re-

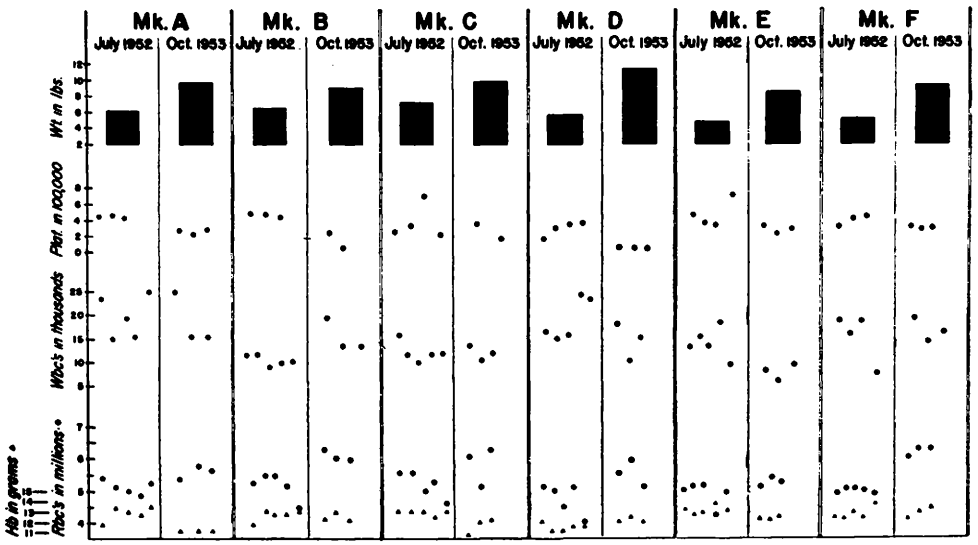

FIG. 1. Prolonged chloromycetin administration to monkeys (750 mg daily; total dosage, 300 g).

ceived a total of 300 g from July, 1952 through October, 1953. All monkeys gained weight on this regime. There were no significant alterations in any of the peripheral cellular elements as compared to the base-line values taken in July, 1952. No bone marrow depression or changes were noted in any of these animals. Similar results were obtained with set 2 (Monkeys G,H) which received 750 mg daily every other week with a total dosage in H of 150 g. Monkey G died after 14 months of drug administration with generalized tuberculosis. However, neither peripheral blood, nor bone marrow examinations were altered as compared to base-line studies. One (J) of the 2 monkeys in set 3 receiving 5 g daily died after 2 months. This animal had begun to refuse feed while on this program but ante and postmortem studies showed no hematologic abnormalities. Similarly, no abnormalities were noted in Monkey I which received a total of 1800 g over a 14-month period. Negative results were also observed in 3 monkeys (O,S,T) receiving 470 mg of chloromycetin palmitate twice daily for 7 months, for a total dosage of 188 g. Monkeys M and Z which were started on chloromycetin daily immediately after receiving 200 r of total body irradiation likewise were not adversely affected by the drug. Monkey M developed a temporary leukopenia between the 2nd and 3rd weeks after irradiation but the peripheral count slowly returned to normal as did that in Monkey Z (Fig. 2) which also had a temporary post-irradiation depression of red cells as well. Similar results were observed in 3 monkeys who after induction of a moderate nutritional cytopenia restored their hematologic equilibrium while on chloromycetin and normal diet. The blood of all of the monkeys in this study showed microbiologic and chemical evidence of absorption of the drug throughout.

Discussion. It is obvious that this series is small and the results preliminary in nature. Ideally, thousands of monkeys would be preferable, but that would not be practicable or economically feasible. Under the conditions of these studies, to date, we have not been able to produce any hemocytotoxic effects in monkeys. For the past 2 years similar intensive studies in patients receiving chloromycetin for disease processes in which the drug was specifically indicated have revealed no untoward hematologic effects. This is in agreement with other observations recently reported(8). There is still a need for a method whereby the potential bone-marrow depressing effects can be established for each new therapeutic agent. Other studies are in progress in this laboratory to attempt to learn why certain individuals have shown hemato-

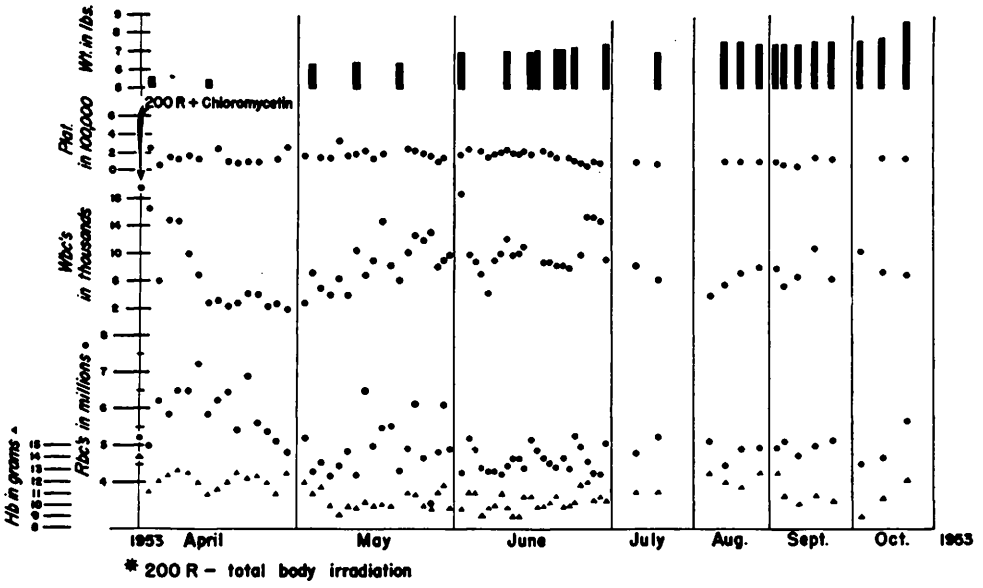

FIG. 2.
Chloromycetin in irradiated monkeys.* Mk. Z (dosage, 750 mg daily; total dosage, 126 g).

logic idiosyncrasies following chloromycetin therapy.

Conclusion. Prolonged administration of chloromycetin did not alter the peripheral or bone-marrow picture in normal, irradiated, or nutritionally cytopenic monkeys.

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