question of the "indirect" effect of radiation. The extensive investigations of Lawrence and his coworkers(11) of lack of effect of cross transfusions from radiated animals into normal have provided strong negative evidence. These studies have been done *in vivo,* whereas the evidence presented here for a plasma clot retraction time inhibitor has been entirely *in vitro.* The inability to demonstrate this factor before the 8th post radiation day is significant because the studies of Lawrence *et al.* extended only through the 5th post radiation day.

Conclusions. 1. There is an inhibition of platelet adhesiveness and a prolongation of clot retraction time following whole body radiation of the dog. These changes are demonstrable 3 days after radiation, prior to thrombocytopenia or prolongation of clotting time which is associated with hemorrhage. 2. Inhibition of clot retraction time can be reversed *in vitro* by addition of excesses of calcium. This suggests a defect in the radiated animal in the use of calcium in initiation of clot retraction. 3. There is a substance in the plasma of the radiated dog which acts on platelets to decrease platelet adhesiveness and inhibit clot retraction time. This factor is not demonstrable before 8th post radiation day and is most easily shown when the animal is thrombocytopenic.

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1. Jackson, D. P., Cronkite, E. P., Levoy, G. V., and Halpern, B., *J. Lab. and Clin. Med.,* 1952, v39, 449.

2. Jackson, D. P., Cronkite, E. P., Jacobs, G. J., and Behrens, C. F., *Am. J. Physiol.,* 1952, v169, 208.

3. Penick, G. D., Cronkite, E. P., Godwin, I. D., and Brinkhous, K. M., PROC. SOC. EXP. BIOL. AND MED., 1951, v78, 732.

4. Jacobs, G. J., and Cronkite, E. P., (Unpublished). Quoted by Cronkite, E. P., and Brecher, G., *Defects in Hemostasis Produced by Whole Body Irradiation. Blood Clotting and Allied Problems,* Trans. 5th Josiah Macy Conference. Josiah Macy Foundation, New York, 1952.

5. Brecher, G., and Cronkite, E. P., *Proc. New York Path. Soc.,* 1950-1951, v116.

6. Woods, M. C., Gamble, F. N., Furth, J., and Bigelow, R. R., *Blood,* 1953, v8, 545.

7. Cohn, S. H., *ibid.,* 1952, v7, 225.

8. Savitsky, J. P., and Werman, R., *Am. J. Clin. Path.,* 1952, v22, 1175.

9. Savitsky, J. P., *Blood,* 1953, v8, 1091.

10. Moolten, S. E., and Vroman, L., *Am. J. Clin. Path.,* 1949, v19, 701.

11. Lawrence, J. S., Valentine, W. N., and Dowdy, A. H., *Blood,* 1948, v3, 593.

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Production of Renal Hypertension by Injection of Finely Divided Silica into Renal Artery.* (20961)

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The frequent occurrence of sustained hypertension in the course of chronic renal disease and the need for a procedure to produce experimental hypertension by an intrarenal lesion occasioned this study. The development of marked fibrosis as a reaction to silica in the liver(1-3) indicated that a similar technic applied to the kidney might produce sustained hypertension.

Methods. Mongrel dogs prepared with an exteriorized carotid artery to permit the ready determination of arterial systolic pressure in the unanesthetized state were kept in the laboratory under uniform conditions. The systolic blood pressure was determined by palpation of the exteriorized carotid distal to an occluding pneumatic cuff at twice weekly intervals for 10 months. After preliminary trials in 24 dogs had established suitable technic and dosage, 5 dogs anesthetized with

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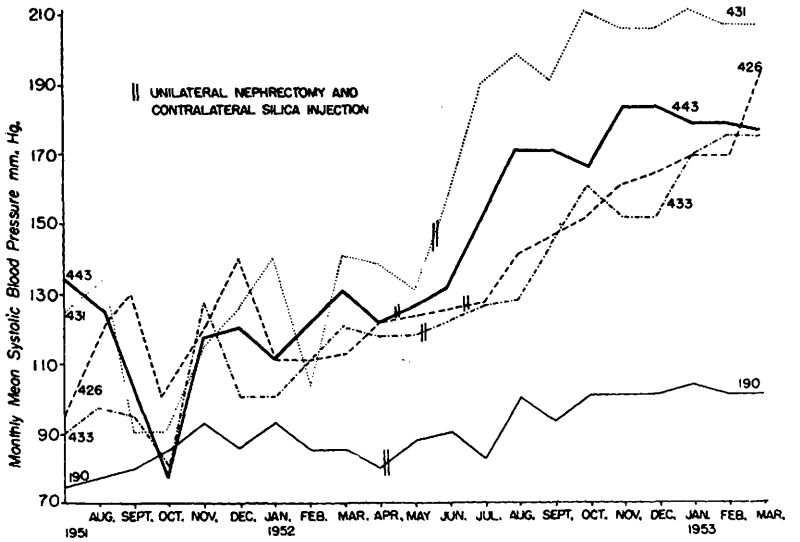

FIG. 1. Monthly mean values for systolic blood pressure in dogs during control period and following unilateral nephrectomy and injection of 5 mg of white silica into the contralateral renal artery.

intravenous pentobarbital were unilaterally nephrectomized, and immediately 5 mg of white silica (0.02 to 0.05 μ) suspended in 2 ml of isotonic saline was injected through a 21-gauge needle into the renal artery of the unoperated kidney as close to the renal pelvis as possible. In 4 other dogs the renal arteries of both kidneys were similarly injected at one operation. Care was taken to have the syringe and needles meticulously clean and the silica suspension freshly made to prevent the jamming of silica in the syringe. Bleeding from the site of the arterial puncture was prevented by finger pressure. In the control and immediate postoperative periods blood urea nitrogen levels were obtained at frequent intervals. After recovery from the operative procedure, the weekly or biweekly blood pressure determinations were resumed. At no time did the observer recording the blood pressure have information as to the operative procedure carried out in the animal under study.

Results. Fig. 1 records the mean values of the systolic pressure that were obtained during each month of this experiment. Fig. 2 records similarly obtained monthly mean values of the systolic pressures in four additional dogs in whom 5 mg of white silica suspended in 2 ml of saline was injected into the renal arteries of both kidneys at the time of laparotomy.

The blood urea nitrogen levels in all animals were normal prior to the silica injection. In the animals subjected to silica injection and contralateral nephrectomy, there was a prompt elevation of the blood urea nitrogen to 35-50 mg % during the postoperative period, but this returned to preoperative levels within 3 weeks. In the animals receiving bilateral renal artery injections a gradual elevation of blood urea nitrogen occurred, reaching a maximum of about 50 mg % at 4 weeks postoperatively and returning to preoperative levels within 8 to 10 weeks.

During the preliminary experimental trials, death from uremia occurred in several animals when 10 or more mg of silica in suspension was injected. With doses of 20 or more mg anuria with uremia and death in 72 hours frequently occurred.

All dogs in this study were sacrificed 8 to 12 months after silica injection. The kidneys injected with silica appeared normal externally. On hemisection there appeared to be diffuse fibrosis of the cut surface with increased prominence of the glomeruli. No hemorrhages were noted. The microscopic sections from all dogs including the 2 that failed to develop hypertension revealed a

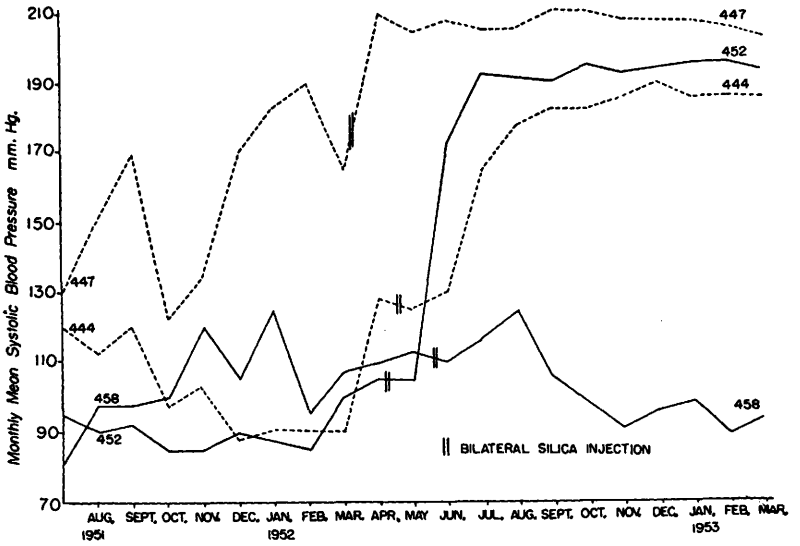

FIG. 2. Monthly mean values for systolic blood pressures in dogs during control period and following injection of 5 mg of white silica into both renal arteries.

diffuse fibrous tissue reaction in the glomeruli with a considerable reduction in the number of functioning units. The tubules were usually of normal appearance, but in a few patchy areas they were replaced by diffuse fibrosis.

Discussion. The wide spontaneous variations in dog blood pressure as determined without anesthesia using the exteriorized carotid (Fig. 1, 2) emphasized the need for an adequate control period in this study. The sustained elevation of arterial pressure, developing in 4 of the 5 unilaterally nephrectomized dogs receiving silica and in 3 of the 4 dogs with bilateral silica injection, indicates that this method may be useful as another method for producing sustained hypertension. The lesion produced by this technic is primarily an intrarenal one and therefore is in some respects similar to the situation in clinical hypertension due to chronic renal disease.

Explanation for the failure of one animal in each group here reported to develop hypertension is not available from this study. The elevation of blood urea nitrogen occurring in these 2 animals was similar to that observed in those developing hypertension, and additional study with determination of renal blood flow, glomerular filtration rate, etc. will be necessary for understanding of the mechanisms involved in this reaction.

Summary. A method for the production of experimental hypertension by the injection of 5 mg of white silica into the renal artery is described. The intrarenal fibrous tissue reaction occurring in response to this injection is apparently responsible for the elevation of blood pressure that occurs.

The white silica used was made by the Linde Laboratories, Tonawanda, N. Y., and provided through the courtesy of Dr. Charles P. Carpenter of the Mellon Institute of Industrial Research.

1. Gye, W. E., and Purdy, W. J., *British J. Exp. Path.*, 1922, v3, 94.

2. Gardner, L. U., and Cummings, D. E., *Am. J. Path.*, 1933, v9, 751.

3. Rousselat, L. M., and Thompson, W. P., PROC. SOC. EXP. BIOL. AND MED., 1939, v40, 705.

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