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Survival Following Acute Coronary Artery Ligation Subsequent to Irradiation of Canine Heart.* (24501)

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Attempts to increase blood supply to the myocardium of the heart with coronary artery disease have been many. The approaches, primarily surgical, have been designed to protect the heart from effects of acute coronary occlusion by promoting intercoronary and extracoronary communications. These methods have utilized foreign irritants, tissue grafts, and various anastomotic and implantation procedures involving systemic vessels and coronary arteries(1). In an attempt to attain the same protective benefits of myocardial revascularization, without the necessity of surgical intervention, the use of cardiac irradiation as a therapeutic measure was investigated. It is our premise that successive small doses of radiation will produce dilatation of existing myocardial capillaries and precapillary arterioles which, in the presence of myocardal ischemia and the natural compensatory ability of cardiac tissue to develop collaterals, will persist and increase in number. To determine the effects of radiation on the canine heart, the following study was performed.

Methods. Mongrel dogs in good health weighing 10-20 kg were used, and divided into Radiation and Control Groups. Each radiation dog received a chest x-ray to determine heart location and size. This field was then mapped on the dog's thorax on both left and right sides. Irradiation was performed by means of 3 treatments to the left chest field and 2 to the right chest field during a 2 to 2½ week period. Treatments were given with a parallel opposing pair of fields ranging from 80 to 120 cm^2. Average separation of fields

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TABLE I. Effects of Acute Coronary Ligation on Survival (If Defibrillation Not Attempted).

Group	Total No. of dogs	No. surviving ligation and alive 24 hr post ligation	% of dogs surviving
Control			
Group A	5	0	0
" B	18	1	5.55
Radiation			
Group 1300 R	15	7	46.66
" 2000 R	18	8	44.44

was 10 cm. 200 kilovolt x-rays, which after filtration had half value layer of 0.9 mm copper at focal skin distance of 50 cm. were utilized. Total dose of radiation to the heart in one group was 1300 Roentgens. The other group received total dose of 2000 Roentgens to the heart. Prior to radiation, each dog was anesthetized with Sodium Nembutal (25-30 mg kg body weight) to insure immobility during treatment. Four to 6 days following last treatment in the Radiation Groups, ligation of the anterior descending branch of the left coronary artery was performed through a left-sided thoracotomy in the fifth intercostal space. An endotracheal tube connected to an automatic respirator, utilizing compressed air, was employed. The anterior descending coronary artery was ligated exactly at its origin from left main coronary artery with 2 OO silk sutures. Sterile procedure was maintained. The thoracic cavity was closed in layers and crystalline penicillin 600.000 units given intramuscularly for 3 days. In the 1300 Roentgen group there was no attempt to defibrillate the animal once ventricular fibrillation developed following placement of coronary ligature. In the 2000 Roentgen group all dogs which fibrillated following ligature were routinely treated with cardiac massage, oxygen, electrical counter-shock, 100 mg of Pronestyl, and .5 mg of Oubain given in stated order and at appropriate time. In none of the dogs were the ligatures removed. To keep conditions equivalent, the control group was also anesthetized 5 times in a 2 to 2½ week period and operated upon 4 to 6 days later. An attempt was also made to defibrillate one group of control dogs. Control Group A—5 dogs. No attempt at defibrillation was made. Control Group B—18 dogs. An attempt at defibrillation was made. Radiation Group 1300 R—15 dogs. No attempt at defibrillation was made. Radiation Group 2000 R—18 dogs. An attempt at defibrillation was made.

TABLE II. Effect of Attempts at Defibrillation in Dogs with Ventricular Fibrillation.

Group	No. dogs which fibrillated	No. dogs defibrillated and alive 24 hr post ligation	% of dogs defibrillated
Control Group B	17	5	29.41
Radiation Group 2000 R	8	7	87.50

Results. The effect of acute coronary ligation on all groups, as measured by survival of animal, assuming that no defibrillation was attempted, is presented in Table I. As this type of fibrillation is not spontaneously reversible, all dogs that fibrillated would have died.

TABLE III. A Comparison of Total Survivors following Acute Coronary Ligation.

Group	Total No. of dogs	Total No. survivors 24 hr post ligation	% surviving
Control			
Group A	5	0	.0
" B	18	6 (includes 5 defibrillated)	33.33
Radiation			
Group 1300 R	15	7	46.66
" 2000 R	18	15 (includes 7 defibrillated)	83.33

Table II presents results when an attempt was made to defibrillate those dogs with ventricular fibrillation in Control Group B and Radiation Group 2000 R without removal of the coronary ligature.

A comparison of total survivors (straight survivors plus defibrillated dogs) is presented in Table III.

Discussion. Analysis of the results significantly indicates that those dogs which received cardiac irradiation prior to acute coronary ligation were less prone to fatal fibrillation following coronary occlusion than the Control Group. Since the entire distribution of the anterior descending coronary artery is

occluded by the ligature applied, it is assumed that prevention of fibrillation occurs by back flow of blood into this area from adjacent coronary vessels. The high mortality in the control group is evidence that this flow is not adequate normally.

Stanton(2) postulates that better survivals, following experimental procedures designed to protect the heart, arise from increased fibrillation threshold which the performance of many of these procedures might induce. Since these dogs have had no operation prior to ligation, one concludes that radiation alone has produced sufficient vascularity to account for the observed differences in survival and increased fibrillation threshold.

Also of interest is the large percentage of radiated dogs which responded to defibrillation without removal of the ligature. Gregg (3) states that "experimentally, in dogs, it is rarely possible to revive a heart with an occluded coronary artery unless the occlusion is first removed and the ischemic area flooded with arterial blood." The experience with the control group tends to indicate that this situation is not as rare as described. However, the percentage difference in ability to defibrillate dogs between both groups and the ease with which defibrillation was performed in the radiated group is of great significance.

Summary. A method of creating increased myocardial vascularity by means of cardiac irradiation has been investigated. On the basis of mortality figures, there is a significant difference between control and irradiated dogs when acute complete ligation of the anterior descending branch of left coronary artery is performed. Ability to defibrillate radiated dogs successfully with the coronary ligature intact is strikingly evident.†

† Histological, physiological and electrocardiographic studies of the effects of cardiac irradiation, now in progress, will be reported.

1. Sabiston, David C., Jr., Blalock, A., *Surgery,* 1958, v44, 406.

2. Stanton, E. J., Schildt, P., Beck, C. S., *Am. Heart J.,* 1941, v22, 529.

3. Gregg, D. E., *The Coronary Circulation in Health and Disease,* Philadelphia, 1950, Lea and Febiger.

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Effect of Dietary Cholic Acid on *in vivo* Cholesterol Metabolism.* (24502)

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The authors have presented evidence(1) which supported the view that effectiveness of dietary cholic acid in promoting accumulation of liver cholesterol in the rat, fed cholic acid and cholesterol simultaneously, is due to ability of bile acids to block cholesterol degradation. Furthermore, in the absence of dietary cholesterol, feeding cholic acid caused only a small accumulation of liver cholesterol, because of simultaneous and equal decreases in rates of liver cholesterol synthesis and mobilization. Inasmuch as in the rat, cholesterol is largely metabolized to bile acids before excretion, these effects could be of major importance in maintenance of cholesterol balances. However, several points must be investigated before this finding can be seen in its true perspective.

The present investigation concerns: 1. Effect of length of time of cholic acid-feeding period on rate of liver cholesterol synthesis; 2. Relationship of serum bile acid concentration to rate of cholesterol synthesis in liver; and 3. Effect of dietary cholic acid on kidney and intestine cholesterol synthesis.

Procedures. Forty-eight Sprague-Dawley female albino rats, weighing 250-280 g were divided into 2 groups. The control group was maintained on basal diet consisting of 97% Ground Rockland Rat Ration and 3% corn

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