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CARDIOVASCULAR RESPONSE OF BEAGLES TO A SUPRALETHAL DOSE OF MIXED GAMMA-NEUTRON RADIATION

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FOREWORD
(Nontechnical summary)

The monkey and apparently man display a period of early transient incapacitation (ETI) after moderately high supralethal doses of radiation (5-10 krads). A marked hypotension has been reported to be associated with the ETI period. Although an ETI period has not been observed in the beagle, CNS symptoms and early permanent incapacitation can occur immediately after supralethal doses of radiation in excess of 10 krads.

It has been shown that head shielding will prevent CNS symptoms and early incapacitation in the beagles receiving a supralethal dose of radiation. The objective of this study was to evaluate the effect of a supralethal dose of radiation on the cardiovascular system of the beagle and to determine if the cardiovascular response could be altered by shielding the head or trunk of the beagle during irradiation.

Eighteen male and female beagles, 2 to 3 years of age and weighing 8.2 to 13.7 kg were used. The animals were divided into three groups, unshielded, trunk-shielded, and head-shielded, with six animals per group. One week before irradiation catheters were surgically placed in the femoral artery and vein. The animals were irradiated with a pulse of mixed gamma-neutron radiation. Unshielded dogs received 19,000 rads to the midline of the trunk and 14,000 rads to the midline of the head. Trunk-shielded animals received 14,000 rads to the head and head-shielded dogs received 19,000 rads to the trunk. The variation of dose between animals within each group was less than 5 percent. The midline tissue dose behind the shield was approximately 6 percent of the midline tissue dose at the same point without the shield in place.

Unshielded and trunk-shielded animals displayed CNS symptoms of nystagmus, convulsions, and copious salivation. No CNS symptoms were observed in the head-shielded beagles.

Immediately after irradiation the blood pressure increased in all groups. This prompt hypertension gradually decreased until by 4 minutes postirradiation near normal values were reached; however, the arterial pressure of the head-shielded group declined further and remained lower than those of the unshielded and trunk-shielded animals. In general, this difference was statistically significant beyond 8 minutes postirradiation. No significant difference among the three groups was found in the blood volume, heart rate, hematocrit, or serum chemistry values studied.

A decrease in the arterial pressure of the beagle has not been observed that is comparable to the acute hypotension which occurs in the monkey after supralethal doses of radiation. It has been reported that shielding the head of the monkey only partially alleviated the acute hypotension or the inability to perform a learned task after irradiation. However, shielding the head of the beagle during irradiation prevented the early incapacitation which occurs in unshielded or trunk-shielded animals. It appears that the early incapacitation observed in the beagle is due mainly to brain damage, whereas damage to both head and trunk structures contributes to the acute hypotension and performance decrement observed in the monkey.

ABSTRACT

Unshielded, head-shielded or trunk-shielded beagles were irradiated with a 19,000-rad midline tissue dose of pulsed mixed gamma-neutron radiation. The cardiovascular response of the beagle and its alteration by shielding were evaluated. Arterial pressure, blood volume, heart rate, and some plasma chemistry values were determined before and for 1 hour following irradiation. Immediately after irradiation the blood pressure increased in all groups. This prompt hypertension gradually decreased until by 4 minutes postirradiation near normal values were reached; however, the arterial pressure of the head-shielded group declined further and remained lower than those of the unshielded and trunk-shielded animals. In general, this difference was statistically significant beyond 8 minutes postirradiation. No significant difference among the three groups was found in the blood volume, heart rate, hematocrit, or serum chemistry values studied.

I. INTRODUCTION

Dogs receiving up to 3000 R of x or gamma radiation showed no significant changes in arterial pressure, blood volume, or hematocrit until within 10 hours of death.[2,5,7-9] Thorp found that beagles which were unshielded or trunk-shielded during irradiation and received 14,000 rads of pulsed mixed gamma-neutron radiation to the head, and in the unshielded animals 19,000 rads to the trunk, exhibited symptoms of central nervous system (CNS) damage within 20 minutes postexposure. No early symptoms of CNS damage were observed in head-shielded beagles that received 19,000 or 25,000 rads to the trunk.[11] Pitchford found that immediate partial incapacitation generally occurred in the beagle at doses of 10,000 to 30,000 rads.[10] Severe hypotension has been reported in man[4] and the monkey[6] during periods associated with early incapacitation.

In the present study the arterial pressure, blood volume, heart rate, hematocrit, and some plasma chemistry values were determined before and for 1 hour after the unshielded, head-shielded, or trunk-shielded beagle received a supralethal dose of pulsed mixed gamma-neutron radiation. The effects of a supralethal dose of radiation on the cardiovascular system of the unshielded and shielded beagles were measured and the contributions of the cardiovascular system to the early incapacitation observed in the beagle were evaluated.

II. MATERIALS AND METHODS

Eighteen male and female beagles, 2 to 3 years old and weighing 8.2 to 13.7 kg, were used in the study.

Catheters were surgically placed in the femoral artery and vein of the anesthetized dog and advanced into the aorta and vena cava. The catheters were run to the top of the shoulders by tunneling under the skin and terminated in a ball valve device which protruded through the skin. The ball valve device was anchored by a larger base under the skin. After surgery the animals were returned to their regular cages where they remained for approximately 1 week before irradiation. The catheters were flushed daily with physiological saline and filled with a heparin-saline solution.

Food was withheld from the dogs for 16 hours before irradiation. Water was available ad libitum. At approximately 1 hour before irradiation the animals were placed in Lucite restraining cages and transferred to the exposure room. The shield, its characteristics, and the methods for dosimetry have been previously described.[11] The arterial catheter was attached to a Statham* transducer for blood pressure determination and the transducer's output recorded by a Sanborn† recorder. The venous catheter was attached to a remotely controlled blood collector containing heparinized glass tubes for the blood. At approximately 20 minutes before irradiation a control sample (8 ml) of blood was withdrawn for plasma chemistry studies. Following the withdrawal of this sample approximately 2.5 μCi of ^{125}I labeled albumin in a volume of 1 ml was injected via the arterial catheter followed by a 1 ml suspension of erythrocytes labeled with approximately 4 μCi of ^{51}Cr suspended in physiological saline. Five minutes before irradiation and at 2, 7, 15, 30, and 60 minutes postirradiation,

* Type P23Db pressure transducer, Statham Laboratories Inc., Hato Rey, Puerto Rico

† Eight-channel recorder, Model 7700, Hewlett-Packard Company, Rockville, Maryland

8 ml of blood were withdrawn for blood volume and plasma chemistry studies. At 45 minutes postirradiation the isotopes were injected as before. At 60 minutes postirradiation the blood sample for blood volume and plasma chemistry determination was collected. The animals were then removed from the exposure room. The unshielded animals were sacrificed after removal from the exposure room. The head- and trunk-shielded animals were observed until 12 hours postirradiation and then sacrificed. All dogs were observed continuously during the study. While in the exposure room they were monitored via closed circuit television. The times of occurrence and the severity of clinical symptoms were recorded.

The unshielded dogs received a midline tissue dose of 19,000 rads of pulsed mixed gamma-neutron radiation to the trunk and 14,000 rads to the head. The trunk-shielded animals received a midline tissue dose of 14,000 rads to the head and the head-shielded animals received a midline tissue dose of 19,000 rads to the trunk. The variation of dose among animals within groups was less than 5 percent. The midline tissue dose behind the shield was approximately 6 percent of the midline tissue dose at the same point without the shield in place.

After the animals were removed from the exposure room the blood was removed from the remote blood collector. Two milliliters of blood from each collection were transferred to glass tubes for blood volume determinations. The technique of Wood and Levitt[12] was used to determine the blood volumes. The remainder of each sample was centrifuged and the plasma decanted for chemistry determinations. The handling, storage, and methods used for the chemical analyses of the plasma have been previously reported.[3]

III. RESULTS

The mean arterial pressure (diastolic + 1/3 pulse pressure) and heart rate before irradiation and for 1 hour postirradiation are plotted in Figure 1.

Immediately after irradiation the blood pressure increased in all groups. This prompt hypertension gradually decreased until by 4 minutes postirradiation near normal values were reached; however, the arterial pressure of the head-shielded group

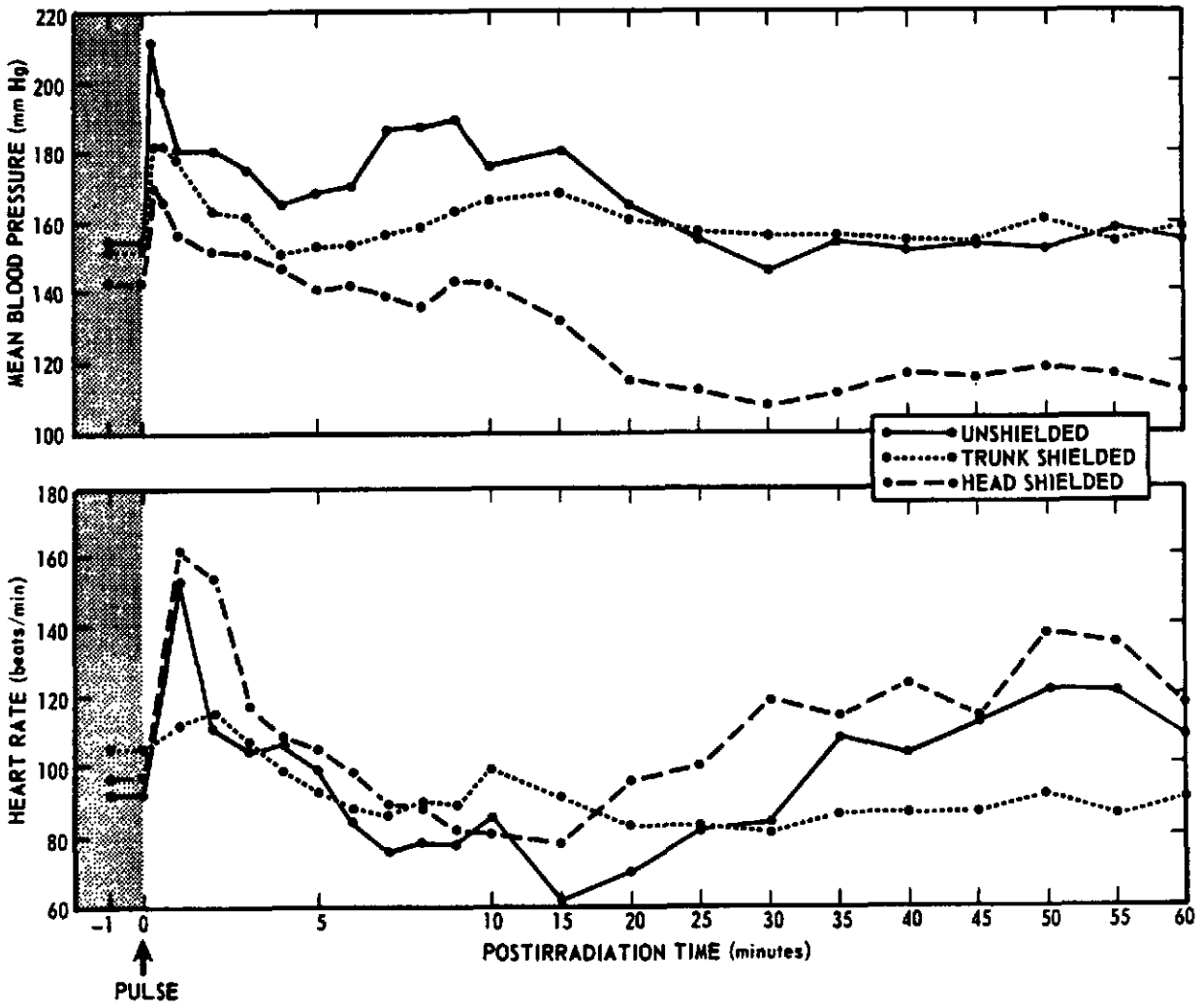

Figure 1. Blood pressure and heart rate of beagles after a pulsed supralethal dose of mixed gamma-neutron radiation (14,000 rads to the head and 19,000 rads to the trunk)

declined further and remained lower than those of the unshielded animals and the trunk-shielded animals. In general, this difference was statistically significant beyond 8 minutes postirradiation.

Considerable variation was observed in the heart rate of animals within the groups after irradiation. No significant difference was found among the three groups.

No significant changes were observed in the hematocrit, cell volume, or total blood volume after irradiation.

The plasma concentrations of sodium, potassium, lactic dehydrogenase, and glutamic oxalacetic transaminase were not significantly different after irradiation from control values previously published for the beagle.[3]

The unshielded and trunk-shielded animals displayed CNS symptoms of nystagmus, convulsions, and copious salivation after irradiation. The head-shielded dogs displayed no CNS symptoms.

IV. DISCUSSION

At present no explanation is offered as to the mechanisms whereby the beagle avoids the prompt, acute hypotension found in man[4] or the monkey.[6] The blood volume was not found to change significantly, as might be expected in an effort to maintain the arterial pressure,[5] nor did the heart rate increase significantly after irradiation. The head-shielded animals were quiet with less movement in the restraining cages after irradiation, whereas the unshielded and trunk-shielded animals were in constant movement and convulsions were frequent. This physical activity may have assisted the latter animals in maintaining arterial pressure at or above their preirradiation values.

When the monkey receives a 15,000-rad dose of pulsed mixed gamma-neutron radiation the arterial pressure begins to decrease within 4 minutes and remains significantly depressed until approximately 20 minutes postirradiation when it begins to return toward normal values.* In the present study, the arterial pressure of the beagle did not decrease significantly after supralethal doses of radiation.

A decrease in the arterial pressure of the dog was not observed that is comparable to the acute hypotension displayed by the monkey after a supralethal dose of radiation. Thorp[11] found that shielding the head of the beagle during irradiation prevented the early incapacitation observed in the unshielded or trunk-shielded animals, whereas Chapman[1] observed that shielding the head of the monkey only partially alleviated the acute hypotension or the inability to perform a learned task after irradiation. It appears that the early incapacitation observed in the beagle after supralethal doses of radiation is due mainly to brain damage, whereas damage to head and trunk structures contributes to the acute hypotension and performance decrement observed after irradiation in the monkey.

* Unpublished: Turbyfill, C. L., Armed Forces Radiobiology Research Institute, Bethesda, Maryland 20014

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Unshielded, head-shielded or trunk-shielded beagles were irradiated with a 19,000-rad midline tissue dose of pulsed mixed gamma-neutron radiation. The cardiovascular response of the beagle and its alteration by shielding were evaluated. Arterial pressure, blood volume, heart rate, and some plasma chemistry values were determined before and for 1 hour following irradiation. Immediately after irradiation the blood pressure increased in all groups. This prompt hypertension gradually decreased until by 4 minutes postirradiation near normal values were reached; however, the arterial pressure of the head-shielded group declined further and remained lower than those of the unshielded and trunk-shielded animals. In general, this difference was statistically significant beyond 8 minutes postirradiation. No significant difference among the three groups was found in the blood volume, heart rate, hematocrit, or serum chemistry values studied.

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