Leukopenic and Thrombocytopenic Effect of Hypothermia in Dogs. (22070)

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(Introduced by G. M. Guest.)
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Serious cardiac arrhythmias and cessation of respiratory center activity are two major complications of hypothermia which have caught the attention of investigators studying the effects of cooling. The purpose of this report is to describe another complication observed in a high proportion of our experiments. Leukopenia and a thrombocytopenia often developed in dogs which were subjected to rapid cooling; this marked reduction in the number of thrombocytes may be related to the hemorrhagic phenomena which were also encountered in many of the animals. During early investigations of hypothermia in this laboratory we noted that a large proportion of the dogs bled from the gastro-intestinal tract during the first 48 hours after rewarming(1). This loss of blood was a complication seen more frequently in the dogs subjected to experiments in hypothermia than in a similar group of animals subjected to major operative procedures with normal body temperature. In the course of another group of hypothermia experiments a second manifestation of this hemorrhagic diathesis was noted. Dogs that were cooled to the range of 18° to 26°C were subjected to exploratory thoracotomy. In most of these animals the surfaces of the wounds oozed blood in a way not observed in the course of operations upon animals with unimpaired coagulation mechanisms. This faulty coagulation was no doubt the cause of the unusually high incidence of hemothorax in the animals which survived the experiment. Several earlier reports mentioned intestinal tract bleeding as a complication in dogs that had been cooled(2,3). While this complication was manifest in more than one-half of the animals cooled in our laboratory, the impression gained from publications is that others have not observed this type of bleeding so frequently. The mechanism of the diathesis has not been explained, although Ross has noted prolongation of the clotting time in his experiments with cooling by an extracorporeal technic(4).

There is also a clinical aspect to this problem. Even though it cannot be stated in absolute terms at this time, it appears that impairment of the coagulation mechanism may develop in patients subjected to hypothermia as currently employed for cardiovascular surgery(5). It seemed advisable, therefore, to plan a group of experiments in rapid cooling with special attention to the effects upon the blood cellular elements, as the first step in an attempt to elucidate the problem of post-hypothermia bleeding in dogs.

Method. The mongrel dogs used were 8 months old or older; those with infection or malnutrition were excluded from the group for these experiments. Excitation of the animals during the administration of the anesthetic was avoided as far as possible. Pentobarbital sodium was administered intravenously in average dose of 250 mg. The trachea was intubated at once. In the more active animals this was facilitated by the administration of small amounts of ether by open drop. Cyclopropane and oxygen were administered thereafter, and this proved to be an ideal anesthetic in all experiments in which hypothermia was induced. However, the animals with normal body temperature in the control series required additional doses of diphenhydramine hydrochloride (Demerol) to maintain anesthesia at a satisfactory plane. All of the dogs breathed actively during the period of observation and no mechanical ventilator was employed. Animals were supported in the prone position, tilted so that the extended hind legs were at a level 6 inches higher than the head. The dorsal surface of the thorax was shaved and cracked ice was

packed about all of the body except the head and neck. Brine was circulated through this loose ice pack to speed the cooling. Additional procedures in the experiments involved only minor surgery. A ligature was passed around the trachea and tied so that no gas escaped around the in-lying tracheal catheter. The venous pressure was measured through a catheter inserted into the superior vena cava. Samples of venous blood drawn after the animal was anesthetized were obtained through the same catheter; the blood was allowed to drip into heparin tubes and syringes were not employed. The blood pressure was measured with a mercury manometer, attached to a cannula in the femoral artery. Temperature changes were measured by a thermometer inserted into the rectum. Samples of venous blood were kept chilled in a pan of cracked ice. The counts of erythrocytes, platelets(6) and leukocytes(7), as well as the preparation of blood smears and determination of hematocrit(8), were completed within 4 hours after the samples were collected.

Results. Control experiments were carried out on 5 dogs. The standardized method for anesthesia was used for this group, but it did not prove as satisfactory as when it was employed in the hypothermia series (see Method). The conditions of the experiment did not vary in any other respect; the animals in the control group had their backs shaved and were subjected to the same procedures as those employed in the hypothermia group for cannulation of the trachea and an artery and vein. Observations were continued over a period slightly longer in the series of control animals than in the group of 19 that were placed in cracked ice. The average period of observation was 157 minutes for the control group and 100 minutes for the group subjected to cooling.

Acidosis which was most likely respiratory in origin, was of comparable severity in both groups of animals. This fact was ascertained by the measurements of pH and carbon dioxide content in samples of arterial blood drawn at regular intervals during the course of the experiments. The average of the lowest rectal temperatures observed in the animals in the chilled group was 24.3°C.

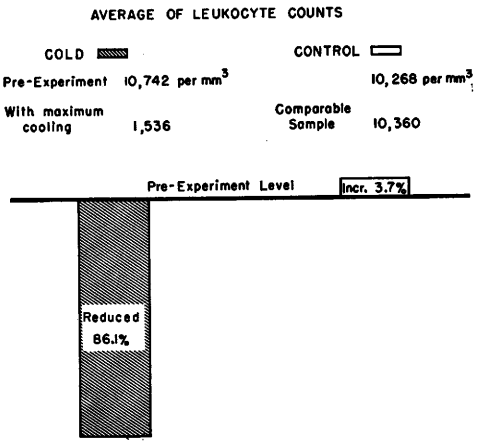

FIG. 1.

Changes in the hematocrit were similar to those that have been reported on many occasions by earlier investigators. The dogs that were cooled had some hemoconcentration with an average increase in hematocrit of 9 vol. %. The mean corpuscular hemoglobin concentration fell somewhat with the average change 1.7%. The mean corpuscular volume increased with the average rise 7.5(9) cubic micra.

There was a marked change in the total leukocyte count produced by hypothermia. Fig. 1 tabulates the averaged results in the cooled group for comparison with the averaged changes in the controls. An 86% reduction in leukocyte count was associated with the lowered body temperature. A differential count of cells was not made from every sample. However, the changes were consistent in all samples that were examined completely. The percentage of lymphocytes in the smears increased and the percentage of neutrophils fell to approximately one-third of the value obtained at normal temperature. The conditions of the control experiments resulted in a small increase (3.7%) in the leukocyte count. This change in the control series is not statistically significant.

The total eosinophil count was also altered in these experiments. In Fig. 2 the results in the hypothermic group are compared with the results from dogs at approximately normal

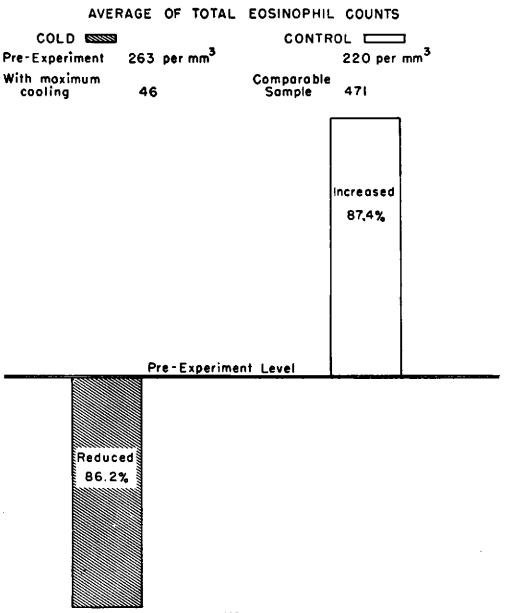

FIG. 2.

body temperature.* The average of the fall in total eosinophil count was 86.2% in the hypothermic group. In the controls, however, this count was increased 87.4%.

Another outstanding change observed in these experiments was in the platelet count (Fig. 3). The change observed in the control experiments was a reduction in the count which averaged 16.5%. The dogs that were cooled had an 81.7% reduction in the count

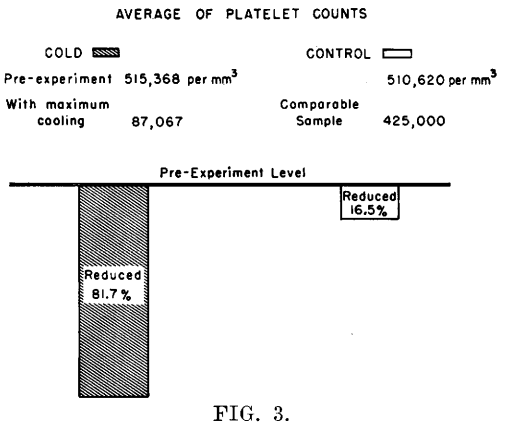

FIG. 3.

* The range of temperatures was from 36° to 37°C. Slight cooling resulted from washing, shaving, and the anesthetized state.

of platelets. In several of the experiments no platelets could be found in the samples of blood drawn at the time of the maximum cooling effect. The samples of blood remained uncoagulated when allowed to stand for two hours in Lee-White tubes at room temperature.

Summary. 1. Attention is drawn to the complication of impaired coagulation encountered in experimental hypothermia in dogs. 2. The method used for anesthetizing and rapidly reducing the body temperature by packing in cracked ice is described. 3. The following changes were associated with hypothermia: The leukocyte count was reduced an average of 86%, the total eosinophil count was reduced an average of 86%, and the platelet count was reduced an average of 81%. 4. The coagulation mechanism was not studied directly, but data from these experiments suggest that the strong thrombocytopenic effect observed may be a factor in the impaired coagulation.

The authors wish to acknowledge the assistance given by Miss Jocelyn Simpson and Miss Joan Hamme in preparation of the manuscript.

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Received October 17, 1955. P.S.E.B.M., 1955, v90.