The copper end of the soldering iron is beveled to a point 1 sq mm in area. The potentiometer provides for point temperatures from 39° C to 85° C. Since the temperature of the skin serves as the zero point, 39° C should serve to localize warm receptors. However, experience has shown that 44° C serves the purpose best. To obtain this temperature on the particular instrument constructed by the authors the potentiometer is set at a dial reading of 4, which means that about 1,800 ohms of the potentiometer are in the circuit. At any rate, the point temperature can be varied to meet the experimental demands by changing the resistance in the potentiometer, to reach the desired temperature.

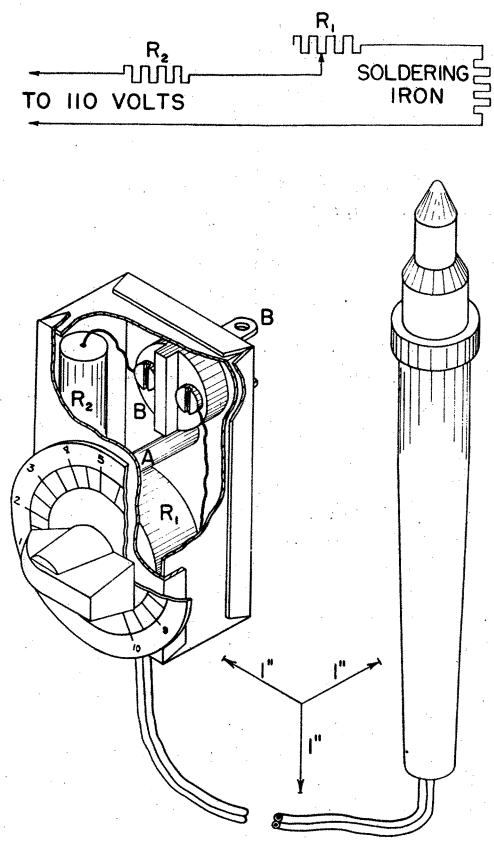

FIG. 2. Apparatus for localizing warm receptors.

The apparatus just described, for the localization of cold and warm receptors, is also suitable for applying cold and heat to any localized area where it is desirable to show the effect of temperature changes on activity. The equipment is effective, readily controlled, and inexpensive. Its simplicity of construction is advantageous in that it can be made available for any laboratory with limited shop facilities.

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Hemophilia in the Female Dog[1]

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The inheritance of true hemophilia as a recessive sex-linked characteristic is well established. Genuine cases of this disease appear to have been observed in the male sex only. However, the disease would be expected in females from matings in which both parents could contribute X chromosomes containing the affected gene *h*. Marriages between hemophilic males (X_hY) and females heterozygous for the disease (X_hX_H) are believed to have occurred on rare occasions. Apparently, true hemophilia did not appear among the female progeny. This lack of hemophilia in the female has been the subject of speculation for decades, and has led to several alternate hypotheses, including the following: (a) the hemophilic gene is sublethal, and a double dose of the gene, such as would be present in a female hemophiliac, is lethal; (b) the genotype X_hX_h may occur, but the bleeding tendency is not manifest in females; and (c) the opportunities for the appearance of hemophilic females have been too limited to determine whether or not this genotype can occur.

Recently a bleeding disease in male dogs was described in which a sex-linked type of inheritance was demonstrated by matings between females, heterozygous for the disease, and normal males (*2*). Extensive studies showed that the clotting defect in the canine disease was indistinguishable from that in human hemophilia (*3*). The untreated bleeders usually died of massive hemorrhage early in life. By frequent transfusions of blood or plasma the hemorrhagic phenomena were controlled, and the bleeder males were reared to maturity.

The purpose of this study was to test the results of mating these bleeder males with females heterozygous for the disease. From such a mating, half of the males should be bleeders. Likewise, half of the females should be bleeders, provided that the disease can exist in this sex. The results of these matings are shown in Table 1. Ten of the 19 female pups tested proved to be bleeders. This was as close to the theoretical expectation of a 1:1 ratio as was possible. In the males, the preponderance of nonbleeders over bleeders, 14 to 8, appears, on application of the chi-square test, to be merely a chance deviation from the expected 1:1 ratio ($\chi^2 = 1.64$; $n = 1$; $P = 0.2 - 0.3$).

Of the ten female hemophiliacs, four died during the first 2 weeks of life. One died of massive hemorrhage, one died accidentally, and two died of undetermined causes not associated with hemorrhage. The remaining six animals vary in age from 2 to 10 months. They were raised under conditions similar to those described previ-

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[2] Markle Scholar in Medical Science.

TABLE 1

PROGENY FROM MATINGS OF FEMALES HETEROZYGOUS FOR HEMOPHILIA WITH HEMOPHILIC MALES*

Litter No.	Pups in litters		Females		Males	
	Total No.	No. tested	Hemophiliacs	Non-hemophiliacs	Hemophiliacs	Non-hemophiliacs
1	15	5	2	0	2	1
2	9	8	2	1	1	4
3	11	11	1	4	2	4
4	9	7	0	3	1	3
5	7	6	4	0	1	1
6	7	4	1	1	1	1
Total	58	41	10	9	8	14

* Four dams and two sires were used in these matings. Two dams had two litters each; litters 2 and 5 were from one dam, litters 3 and 6 from another dam. Animals not tested were either stillborn or died during the first 2 days of life. In litter 1, dam suffered from dystocia, and only the first few pups were viable.

ously (*3*). All of them have suffered from many hemorrhagic episodes, particularly hemarthroses and subcutaneous hemorrhages. The joint hemorrhages have recurred frequently, and in the two oldest animals permanent joint deformities have resulted. Repeated transfusions of normal plasma, in amounts varying from 2 to 4 ml/kg body weight, have served to control the hemorrhagic manifestations, and no animal thus treated has died.

TABLE 2

CLOTTING STUDIES ON FEMALE BLEEDER DOGS*

Dog No.	Clotting time (Lee-White)	Bleeding time (mucous membrane)	Prothrombin utilized during 1st	Clotting time 15 min after transfusion
	min	min	%	min
1	70	2½	0	9
2	61	1½	2	..
3	56	2	0	7½
4	60	2	0	6
5	120	2	0	8
6	110	1½	0	7
Normal Control	5½	1¾	>90	..

* Methods used in these tests were described previously (*3*). Transfusions consisted of normal citrated dog plasma given in a dose of 3 ml/kg body weight.

Table 2 shows the results of one group of clotting studies on the female bleeder dogs. All of these animals showed prolonged clotting time, normal bleeding time, delay in prothrombin utilization in shed blood, and a normal or nearly normal clotting time following transfusions of normal plasma. These findings, along with other studies, indicate that the female bleeders differ only in sex from the hemophilic male dogs previously described (*3*). Like human hemophiliacs (*1*), they appear to be deficient in a plasma factor required for platelet utilization and mobilization of thromboplastin.

As far as can be determined, these animals are the first cases of true hemophilia in the female. That the genotype X_hX_h is not a lethal combination, at least in dogs, is of considerable interest. Indeed, the close approximation of the observed incidence to the expected incidence of this genotype suggests that there is no tendency toward prenatal lethality. Our findings suggest that the lack of female hemophilia in humans is due to the paucity of matings between female heterozygotes and hemophilic males.

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Diabetogenic Effect of Dehydroglucoascorbic Acid[1]

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Dehydroascorbic and dehydroisoascorbic acids have been shown to produce diabetes (*7*, *8*). They are believed to be the only substances of known chemical structure, other than compounds related to alloxan, that will produce lasting diabetes after administration of a few doses. It seemed important to investigate the possible diabetogenic action of related compounds. Therefore, diketogulonic and dehydroglucoascorbic acids were selected for study in rats.

Diketogulonic acid was obtained by permitting dehydroascorbic acid, prepared by the oxidation of L-ascorbic acid with quinone (*8*), to mutarotate at room temperature for 14 days (*10*). Just before injection into the rat, the acid was neutralized to pH 6.7 with 2*N* NaOH. Neutralization required one equivalent of alkali. The product is stable at this pH (*2*). Dehydroglucoascorbic acid was prepared by oxidation of D-glucoascorbic acid[2] with quinone as previously described (*8*).

Six male rats of the Sprague-Dawley strain, ranging in weight between 98 and 130 g, were given intravenously 17.7 millimoles of diketogulonic acid per kg following 48 hr of starvation. The rats showed no hyperactivity, lacrimation, or increased salivation after the injection. Blood sugars were determined on six occasions during the 2 weeks following injection, and there was no hyperglycemia in any of the animals. The rats gained weight normally during this period.

Another series of male rats of the Sprague-Dawley strain were injected intravenously with dehydroglucoascorbic acid following 48 hr of starvation. After the injection there was no hyperactivity, lacrimation, or increased salivation. With a dose of 8.5 millimoles per kg,

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