Initially sucrose was pleasant at all concentrations to fasting normal subjects (*3*). After glucose ingestion, the sweet sensation became unpleasant, developing with time and varying from subject to subject (*2*) (Fig. 1). When sucrose at the concentration of 20 g per 100 ml of solution became unpleasant, all other concentrations tasted also were unpleasant in most cases (Fig. 2). The difference between affective response for sucrose before and after glucose ingestion is statistically significant ($.05 > P > .02$) (*4*).

In obese patients, the gastric glucose load also changed the affective preference for sucrose (Figs. 1 and 2), but to a much smaller extent, and the sucrose stimulus after glucose did not become unpleasant at any of the concentrations offered. The difference in responses before and after glucose load in obese subjects was not statistically significant ($P > .05$) (*4*).

Obese patients, unlike the nonobese controls, seemed to feel very little difference between the pleasantness of the taste of sweet solutions before and after glucose loads. These data lend support to the theory that obese people are generally unaware of internal signals for control of food intake. It is not known whether this phenomenon is a cause or a result of obesity (*5*).

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5. The averages after glucose load given in Fig. 2, as well as the statistical analyses, include: of the ten control subjects, one gave a typical "obese" response; and of the 15 obese, two subjects gave normal responses. We suggest that these "exceptions" may not be atypical for their groups if their past or future case histories are studied. Indeed, such "anomalous" results may prove to have predictive value.
6. We thank M. Plauchu and R. Mornex (as well as the subjects themselves) for permitting the observation of obese patients, and C. Bizollon for the quantitative analyses of the blood samples for glucose and insulin.

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Summer Hibernation Induced by Cryogenically Preserved Blood "Trigger"

Abstract. *Summer hibernation induced by transfusions of blood (serum, cells, or whole blood) from hibernating ground squirrels and woodchucks demonstrates that (i) this "trigger effect" can be preserved cryogenically in vitro for at least 5 months, (ii) it cross-reacts between these species of hibernators, and (iii) its effectiveness relates to the donor's previous hibernation history.*

In January of 1969 an experiment was reported (*1*) in which the blood of hibernating ground squirrels (*Citellus tridecemlineatus*), transfused into active ground squirrels, produced hibernation serially in summer months. That experiment had been performed in 1968. We report now on our 1969 efforts to reconfirm and extend this observation.

Our experimental approach was threefold. In the first instance, we endeavored to discover how a pattern of hibernation in both the donor and the recipient may affect the phenomenon we had observed. Second, we wished to know whether or not the "trigger" for hibernation, which exists in hibernating blood, can be preserved intact cryogenically. Third, an answer was sought to the question of whether hibernating woodchuck (*Marmota monax*) blood would trigger hibernation in the ground squirrel. A series of experiments was carried out addressed to these problems. This report divides into two subsections: (i) blood directly transfused, experiment involving cold- and warm-adapted animals, and (ii) blood cryogenically preserved, stored blood transfusion experiment.

Blood directly transfused. On 26 March 1969, in each of seven cases, approximately 1 ml of blood taken from a hibernating ground squirrel [following a procedure identical to that described previously (*1*)] was transfused into the saphenous vein of an active ground squirrel which was then placed in the cold room (7°C). Four of these animals had been kept in the warm room (about 20°C) throughout the previous winter and had not hibernated. The other three had lived in the cold room throughout the previous winter and also had not hibernated. It should be noted that these three were aberrant cold-adapted animals (in contrast to most of our animals in the cold room which had hibernated at one time or another), since they were cold-adapted, nonhibernating hibernators. The results of this experiment are describable quite simply: the four transfused warm-room animals went into hibernation within the next 22 days, whereas the three transfused cold-room animals did not enter hibernation for at least 100 days thereafter. One of the warm-room animals that hibernated died 24 days after the transfusion (having entered hibernation 10 days after transfusion).

Inspection and treatment of data on the four transfused animals that hibernated gave three relations of interest. These are shown in Figs. 1 and 2. Briefly, the data indicate: (i) The number of days in which the donor animal was in hibernation at the time of exsanguination was inversely and logarithmically related to the length of time in days required for the recipient warm-room animal to enter hibernation (Fig. 1). (ii) Cold-adapted recipients did not hibernate following transfusion, whereas warm-adapted animals did hibernate (Fig. 2). (iii) The percentage of time that an animal spent hibernating in the 60-day period following transfusion was directly related to the percentage of time in hibernation shown by the donor animal during the 60-day period prior to its exsanguination (Fig. 2).

Blood cryogenically preserved. Basically, this experiment consisted of withdrawing bloods on 20 January, separating cells and serum in some cases, and freezing all samples in liquid nitrogen (*2*). The same procedure was followed on 21 February. These blood

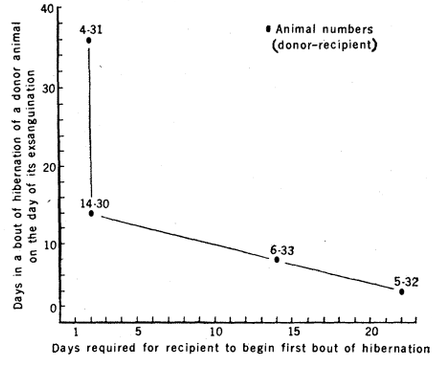

Fig. 1. This figure shows how soon the recipient began hibernation following direct transfusion on 26 March 1969.

Table 1. Midsummer cryogenic experiment. A indicates the number of animals that were transfused; B, the number (in group A) that hibernated in 60 days after transfusion. All transfusates were thawed to 5°C.

Donors	Recipients transfused with									
	Whole blood		Red cells		Serum		Saline		Totals	
	A	B	A	B	A	B	A	B	A	B
Experimentals										
Hibernating ground squirrel	5	5	8	7	10	8			23	20
Hibernating woodchuck	2	2			1	1			3	3
Controls										
Active ground squirrel	4	0							4	0
Saline							6	1	6	1

samples were kept at liquid-nitrogen temperatures for 4 or 5 months (until 20 June) when they were thawed to 5°C and transfused. Pertinent results in recipients receiving transfusions of thawed, cryogenically preserved blood (whole blood, washed cells, or serum) from hibernating hibernators and from nonhibernating hibernator controls, as well as saline controls, is contained in Table 1. The table shows that of the 26 animals transfused on 20 June with thawed, cryogenically preserved blood from hibernating animals, 23 began hibernation during the 60-day midsummer period after transfusion. Of ten control recipients that had been transfused with thawed active blood or with cold saline, only one hibernated. (However, this latter hibernation lasted for 1 day only.) The number of days required for successfully induced recipients to begin a first bout of hibernation varied from 2 to 53 days, most beginning hibernation between the 26th and 37th days after transfusion. No correlation in recipients was observed between time of catch (spring caught or fall caught), cold adaptation (warm room or cold room), or sex. For the donor, no correlation was established either between length of bout of hibernation prior to exsanguination, the month the blood was drawn and time stored (20 January versus 21 February), the use of whole blood, washed red cells, or serum and the induction of hibernation. A remarkable correlation did exist, however, in three situations involving nine animals, wherein donor blood from a single hibernating animal administered to two different recipients induced hibernations on the same day. One of the three situations serves as an example: 1 ml of washed red cells from hibernating ground squirrel donor No. 23 and 1 ml of serum from the same animal induced hibernation in recipients No. 57 and No. 67—exactly on the 35th day after transfusion.

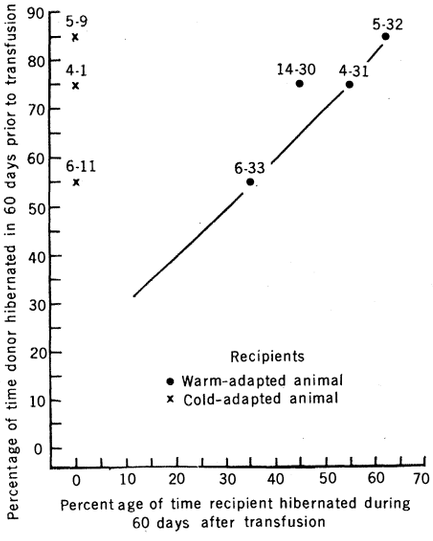

Fig. 2. This figure shows how well the recipient hibernated following direct transfusion on 26 March 1969.

Finally, it should be noted that no animals showed symptoms of anaphylactic shock or other adverse reactions to transfused blood, whether such transfusion was isologous or heterologous.

Four questions and the answers that this research affords are:

1) Is the "trigger" to be found exclusively in serum or in cells? The data provided no satisfactory answer to this question, since regardless of whether the recipients received hibernation serum, cells, or whole blood they apparently randomly hibernated within 60 days after transfusion.

2) Is the "trigger" inactivated with time (particularly following removal of blood from the donor animal)? Three facts appear. (i) Certainly it is shown here that it can be retained in vitro cryogenically for at least 5 months after exsanguination. (ii) The fresh blood transfusions of 26 March indicated that effectiveness in terms of induction times appeared to be causally related to length of time in hibernation of the donor during its last bout of hibernation prior to exsanguination. This argues that measurable time is needed for the donor to produce a significant concentration of effective "trigger" substance in the blood. (iii) It takes different times for the same blood to act in recipient animals but with the three remarkable exceptions noted above. Thus, effectiveness is related to donor titer, capability for storage, and recipient susceptibility. Its action cannot, however, be said positively to be hormonal, except insofar as it may set in motion a prehibernatory process. Such a process may take a measurable time to finalize. This, in turn, may depend upon conditions of this recipient, particularly its time in a biorhythmic cycle (circadian, circannian, and others).

3) What effect does acclimation to cold of a recipient have on the effectiveness of the "trigger"? An answer provided by the 26 March experiment (see Fig. 2) appears to be that cold acclimation per se in these animals acts to prevent hibernation from occurring; that is, the "trigger" is rendered ineffective. However, in the cryogenic experiment, no such relation exists, since cold-room animals apparently hibernated as well as warm-room animals. An explanation for these facts may be that the experiment in which fresh blood was used involved use of cold-room recipients with a history of poor hibernation, whereas the cryogenic experiment utilized animals that had a good hibernation history during the previous winter.

4) Is the trigger species-specific? The answer seems unquestionably to be "no" since all three of the recipient ground squirrels receiving donor hibernating woodchuck blood in fact hibernated.

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