tained on day 7. This volunteer experienced multiple paroxysms with maximum fever of 40.8°C and maximum parasitemia of 3450 parasites per cubic millimeter of blood. This infection was terminated with antimalarials because of the occurrence of daily fevers due to multiple asexual cycles of the parasite. However, before treatment, the parasite was blood-passaged to another volunteer, who developed patent parasitemia by day 6. The infection in this volunteer exhibited a quartan fever pattern through four consecutive paroxysms, after which daily fever was observed. Maximum fever of 40.4°C was observed on day 10 and maximum parasitemia of approximately 10,000 parasites per cubic millimeter on day 14. It is considered that the course of parasitemia and the clinical illness observed in the latter two volunteers are typical of *P. malariae* infections in man and would rule out the possibility that a quartan parasite of the owl monkey might have been inadvertently transmitted. The establishment of this strain of *P. malariae* in a small nonhuman primate and its transmissibility through the mosquito further indiate the usefulness of the owl monkey in research in human malaria.

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Thermoregulatory Responses to Intra-Abdominal Heating of Sheep

Abstract. *When electrical heat sources were implanted in the abdominal cavities of sheep and heated to dissipate 20 to 22 watts of additional endogenous heat in the animal, a rapid increase in respiratory frequency and respiratory water loss occurred 3 to 5 minutes after the initiation of heating. The response was accompanied by a marked decline of the temperature of the hypothalamus, with an increase of less than 1.0°C in skin temperature over the location of the heaters in the abdomen. When the same skin area was heated externally in the absence of internal heating, no significant response was seen. The results support the concept of the existence of thermoreceptors, located in deep tissues or veins, which play a role in the regulation of body temperature.*

The regulation of the body temperature of homoiothermic animals is thought to be mediated largely by a dual system of neural control involving the hypothalamus and peripheral skin thermoreceptors. Evidence has been accumulating that there is a third major factor in the integrating system responsible for body temperature regulation, namely, deep body thermal receptors (*1*). There have been few direct observations, however, to support the concept of deep temperature receptors. Techniques have been developed in this laboratory to aseptically introduce electrical heat sources at various sites within the animal body and leave them for long periods of time to provide a method for the study of the effects of additional internal heat (*2*) and how they may relate to the effects of heat from an artificial heart. Such stimuli, administered in conjunction with standard procedures for the study of thermoregulatory activity, constitute a means of studying the deep temperature receptor problem.

In recent studies on sheep designed to determine the general physiological effects of additional endogenous heat, we have found that marked thermoregulatory responses occurred upon heating of the viscera and abdominal wall. Additional endogenous heat was introduced over an area of 150 cm^2 between the viscera and abdominal wall of sheep (*3*) while temperatures at different sites, the metabolic rate, and the thermoregulatory responses of respiratory evaporative heat loss and respiratory frequency were monitored.

Figure 1 is a graph of data recorded when a ewe (41 kg, closely sheared) was endogenously heated while being exposed to a constant environmental temperature of 20°C. With intra-abdominal dissipation of 22 watts of heat during a 30-minute period (designated by the arrows labeled *endo* in Fig. 1), there occurred a rapid increase in respiratory evaporative heat loss of 0.5 watt per kilogram of body weight as shown in the curve labeled *HE*. Respiratory frequency, labeled *RF*, increased twofold during the heating period. The most important response at this time was the rapid decline of the temperature measured in the hypothalamus, T_{hypo}, whereas vaginal temperature, T_v, did not change significantly. It has been demonstrated conclusively that cooling the hypothalamus of the mammal causes the animal to respond in a physiological manner that will reduce body heat loss; for example, in the dog, panting will cease, and the blood vessels of the ears will constrict. In our experiments, however, respiratory frequency increased while the hypothalamus was cooling. In the light of our present knowledge regarding the mechanisms of body temperature regulation, the phenomenon could only occur if the respiratory center were driven to increase its activity by signals from heat-sensitive receptors outside the hypothalamus. This is the case when sufficient skin area is heated and thermally sensitive skin receptors initiate appropriate thermoregulatory responses. In our experiments, the temperature of the skin directly over the heaters located beneath the body wall increased approximately 1°C during the endogenous heating period (Fig. 1). When this same skin area was heated 1.5°C by externally applied electric heaters (designated by the arrows labeled *exo* in Fig. 1), no response in the respiratory frequency or deep body temperatures was noted. At 160 minutes in the experiment, the internal heating was repeated for a slightly shorter period, and a similar response of less magnitude occurred as before. Measurement of skin temperatures at selected sites over the rest of the body surface (not shown in Fig. 1) indicated there were no significant changes in temperature at these points during the experiment.

Throughout the time course of these

experiments, the oxygen uptake by the animal was continuously monitored. These data, computerized to give a continuous reading of metabolic rate, are plotted at the bottom of Fig. 1. The metabolic heat production was constant at a normal resting level, an indication that the sheep was neither periodically restless nor excited by the internal heating—either of which could cause an increase in respiratory frequency.

An increase in respiratory frequency will produce a greater evaporative cooling effect on the venous return. The selective decline of the hypothalamic temperature without a decrease in deep body temperature (measured in the vagina) could be due to countercurrent heat exchange between the blood supply from the carotid artery to the brain and the venous blood returning from the nasal passages. Daniel *et al.* (*4*) have described an intracranial carotid rete in the sheep located in the cavernous sinus to which Baker and Hayward (*5*) have ascribed a thermoregulatory function in brain temperature control. The functioning of this anatomical heat exchanger is believed to be responsible for the depression of the hypothalamic temperature observed.

The results of the experiments described here support the idea that the internal heat stimulus promoted a thermoregulatory response which results in the loss of body heat, a response not dependent upon thermal stimulation of heat-sensitive neurons in the skin or hypothalamus. The blood from the body wall and viscera adjacent to the electric heat sources drained into the large veins of the abdomen and finally into the posterior vena cava. It is evident from the measurement of skin temperature over the heaters that the venous drainage from the heated area underwent an increase of at least 1°C in temperature, a magnitude quite adequate to stimulate thermally sensitive receptors that may lie in the body wall, visceral organs, or in the walls of the large veins.

From the evidence presented, we conclude that thermally sensitive neurons located within the deep tissue or veins of the abdomen were stimulated by the internal heating to drive a physiological heat loss response, and that the drive was sufficient to override, at least for the short heating period, the counterdrive that usually would obtain from the cooling of the hypothalamus. The thermally sensitive neurons may play a role in the control of body temperature, their output may provide information regarding the temperature level of deep tissues of the body—information that would not otherwise be available until warmed, recirculated blood affected thermoregulatory neurons of the brain.

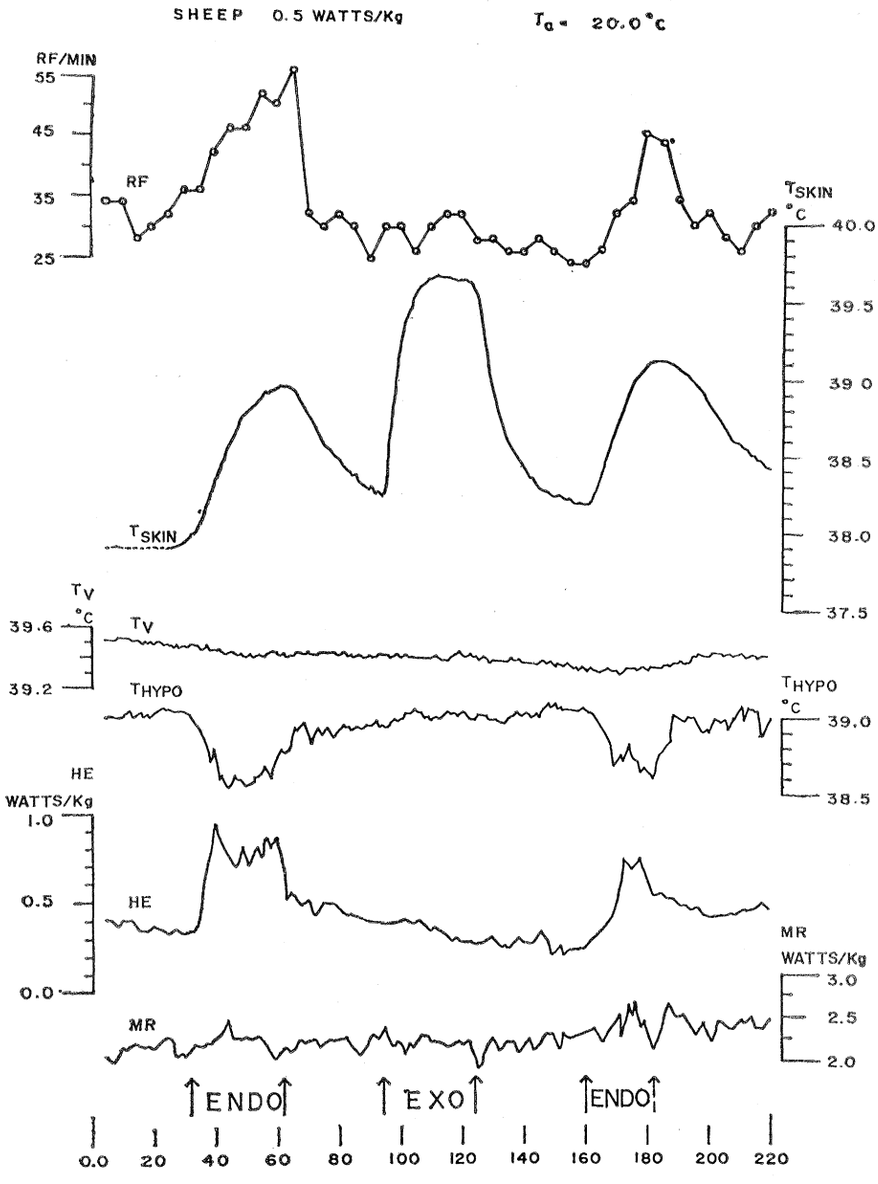

Fig. 1. Response of hypothalamic temperature and respiratory evaporation to intra-abdominal heating of a 41-kg sheep. Plotted in order from top of figure: *RF*, respiratory frequency in breaths per minute; T_{skin}, average skin temperature directly over intra-abdominal heaters; T_v, temperature 15 cm within vaginal canal; T_{hypo}, temperature of hypothalamus; *HE*, respiratory evaporative heat loss; and *MR*, metabolic rate in watts per kilogram of body weight. *Endo* and *exo* designate periods of internal and external heating, respectively.

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