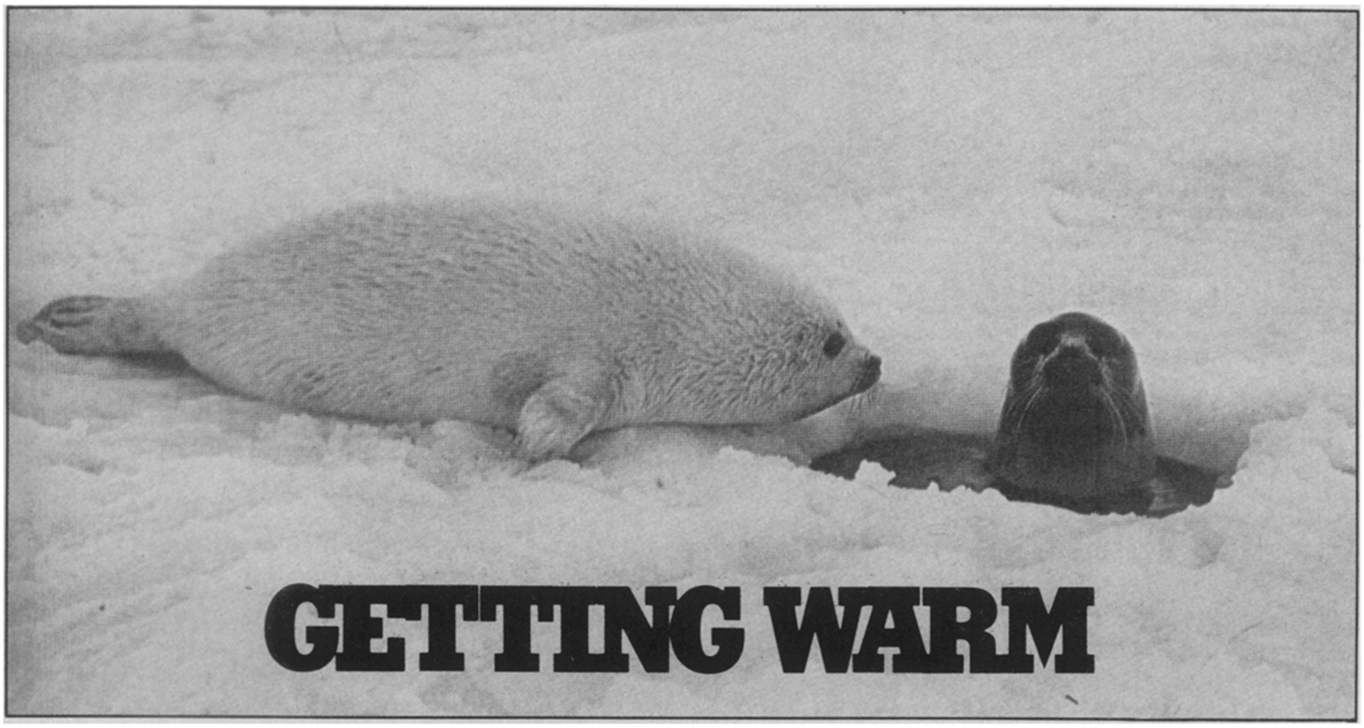


GETTING WARM

Grzimek's Animal Life Encyclopedia

Newborns, hibernators and cold-acclimated small mammals can produce heat with nary a shiver

BY JULIE ANN MILLER

Birth is a cold shock to harp seal pups. They come into a world of windy ice floes and −30°C temperatures. They are naked of the protection adult seals hoist against the arctic chill. The newborns have no layer of blubber and their baby fur when wet does not keep out the cold. These infants do not even seem to shiver. The baby harp seals are protected from the cold only by a little-understood alternative means of heat production, which researchers call nonshivering thermogenesis.

Most warm-blooded animals control their body temperatures with a variety of mechanisms. Some means simply conserve heat, such as a cat's fluffing up of its fur. Shivering is the major mechanism that actually generates heat. For many years physiologists vigorously debated whether another source of extra body heat existed. Now it is clear that under special circumstances many mammals do have a second furnace from which they can draw.

Nonshivering thermogenesis produces heat from an increase in metabolic rate. This mechanism is important in situations where animals must generate warmth suddenly and rapidly, for example, at birth. Researchers have measured significant amounts of nonshivering thermogenesis in newborns of many species, including humans and harp seals. This ability, however, is often lost in adults.

Rapid heating is also required when animals come out of hibernation. When hibernating bats are aroused, nonshivering thermogenesis supplies 80 percent of their metabolic heat, according to the research of John S. Hayward and Charles P. Lyman at Harvard University. In contrast, the dormouse, which is aroused much more slowly, gets only 20 percent of its heat from nonshivering thermogenesis.

Acclimating to the cold is the other situation where nonshivering thermogenesis is important. Heat production from that mechanism is most frequently used by small mammals and is less important in large animals. In small mammals, nonshivering thermogenesis produces about the same amount of heat as does shivering, says Ladislav Jansky, a Czechoslovakian physiologist who has been studying the phenomenon for many years.

Although the details of how this heat production is controlled are still being worked out, the researchers agree that the sympathetic nervous system (the nerves going to smooth muscles and glands) is responsible. Catecholamines, chemicals released from the nerves, switch on nonshivering thermogenesis in response to cold. When animals are cold-acclimated, their response to these chemicals is always greatly enhanced. In rats kept at 4°C for three weeks, the increase in heat production in response to catecholamines is four times that in control animals.

"There are two main sites of nonshivering thermogenesis," says Canadian biochemist Jean Himms-Hagen of the University of Ottawa. They are skeletal muscle and a special kind of fat, called brown adipose tissue. The relative importance of these two sites of nonshivering thermogenesis varies with the animal and its situation. In cold-acclimated adults, the extensive mass of skeletal muscle is probably the most significant source of nonshivering heat. In newborns, however, the brown fat seems to be more important. D. Hull and M. M. Segall at Oxford University found that removing about 70 percent of the brown adipose tissue from newborn rabbits reduced their response to cold by more than 80 percent. In adults, removing the brown fat has a smaller, delayed effect.

"Brown adipose tissue," Himms-Hagen explains, "is specialized for thermogenesis and is generally abundant in those species and under those conditions in which nonshivering thermogenesis occurs." The tissue was first described in marmots, burrowing rodents, in 1551 and was then identified with hibernation. The newborn harp seals, which have so great a need for heat, have an unusual sheet of yellow-brown fat 2 to 8 millimeters thick below the skin. The infant seals also have the more common sheets of fat near the heart and deposits of fat in the neck, observed Norwegian researchers H. J. Grav, A. S. Blix and A. Pasche. Brown fat is most commonly found in the thorax, although its location varies somewhat depending on the species and age of an animal.

Physiologists Robert E. Smith and Barbara A. Horwitz of the University of California at Davis describe brown fat as "an internal heating jacket that overlies parts of the systemic vasculature and on signal becomes an active metabolic heater ap-

Above: Fur of baby harp seal (on ice) provides less insulation from cold than fur of adult. Metabolic heat of nonshivering thermogenesis keeps the pup warm.

plied directly to the flowing bloodstream as it passes to and from the cooler periphery."

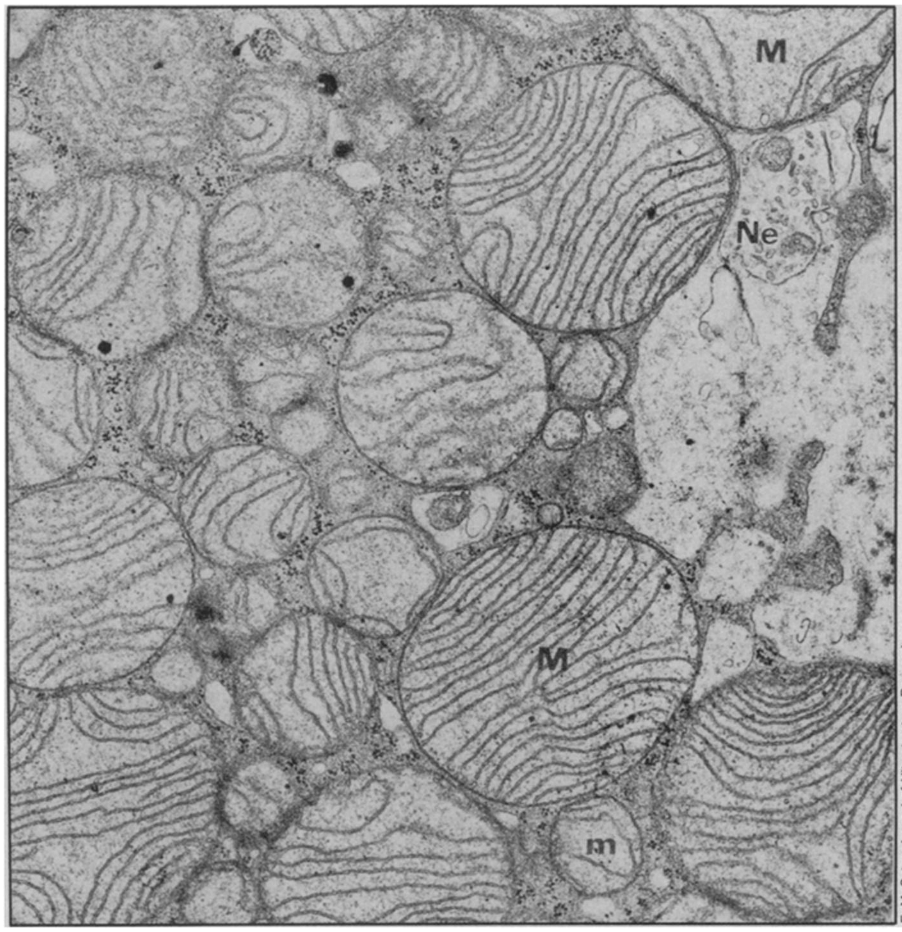
"The cells of brown adipose tissue carry an extraordinary potential for metabolic power," say Smith and Horwitz. Brown fat cells contain an unusually high number of mitochondria, the structures that act as the respiratory power plants of cells, converting oxygen and metabolites into ATP and heat. Furthermore, brown fat mitochondria contain internal membranes that are more tightly folded than is usual. The tight packing of membrane allows more surface for enzymatic operations.

Biologists are particularly interested in the brown fat mitochondria because their major contribution to an animal's physiology seems to differ from that of other mitochondria. "This organelle, which has always requested its structure to be able to transfer electron-carried energy into covalent bonds with high energy of hydrolysis, is used in brown adipose tissue for the theoretically much simpler problem of producing heat," explain Olav Lindberg of the University of Stockholm, L. L. Bieber of Michigan State University and J. Houstek of the Czechoslovak Academy of Sciences. "The mitochondrion represents a very old step in biological evolution. Presumably, once this delicate machinery was designed, it was operable in such a manner that it could be ubiquitously utilized."

Researchers are trying to uncover the special features of mitochondria and other cell structures that produce nonshivering thermogenesis. Much of the work has examined changes during cold acclimation of rats. "There are no metabolic pathways known which are unique to nonshivering thermogenesis," Himms-Hagen and colleagues say. "The problem is, therefore, to explain why known metabolic pathways operate more rapidly in response to stimulation by catecholamines in cold-acclimated rats."

Both the morphology and protein metabolism of mitochondria seem to be altered when rats adapt to the cold, but the changes are different in the two types of tissue so far clearly involved in nonshivering thermogenesis. In brown adipose tissue, during cold acclimation, researchers found increases in the number of mitochondria per cell, in the size of each mitochondrion, in the number of internal membrane folds and in the activity of several mitochondrial enzymes. They found, too, that the rate of protein synthesis, measured as incorporation of a radioactive amino acid, was increased.

On the other hand, in skeletal muscle, Himms-Hagen and co-workers discovered a doubling of the number of mitochondria per cell but a decrease in the size of the individual structures, so that the total mitochondrial mass remained the same. Furthermore, incorporation of the amino acid decreased, rather than increased, during cold exposure.



Large (M) and small (m) mitochondria in brown fat cell of rat acclimating to cold.

"Thus, several lines of evidence point to an altered mitochondrial protein metabolism in brown adipose tissue and skeletal muscle in association with the development of the cold acclimated state," Himms-Hagen and colleagues conclude in BIOCHIMICA ET BIOPHYSICA ACTA (428:599 (1976)). But the exact relationship between these mitochondrial changes and adjustments to cold is not yet known.

The details of how the mitochondria are stimulated is currently the subject of a big debate. Because mitochondria are not completely efficient in producing ATP, they always give off some heat as a byproduct. Horwitz and co-workers believe that catecholamines, the chemical signal from the nervous system for a cell to begin producing more heat, increase the cell's need for energy by making its membrane more leaky to ions. As the cell's mitochondria work to produce ATP for running the membrane pump, they also provide cellular heat. It is as if a piece of machinery were to run at top speed so that the friction of its moving parts would warm the factory.

The other school of thought on the mechanism of heat production holds that catecholamines actually decrease the efficiency of mitochondria, so that more byproduct heat is produced during nonshivering thermogenesis. Or, in the factory analogy, the equipment is readjusted to have more friction and produce more heat.

"Thus, under the influence of thermal stress, the energy transduction machinery of brown adipose tissue mitochondria is regulated to permit a major portion of the oxidative energy of fatty acids to be 'wasted' as heat," Norwegian researchers Torgeir Flatmark and Jan I. Pedersen explain. "However, when this waste is viewed in the context of the whole organism, it is seen that the activity of this tissue provides an effective and rapid means for promoting homeothermy [body temperature maintainance]."

Lindberg and other researchers have proposed that the decreased efficiency, called uncoupling, of the mitochondria is regulated by free fatty acids in the cell cytoplasm. So far, however, no one has successfully detected changes in fatty acid levels during cold acclimation.

The uncoupling hypothesis seems to apply only to brown fat. Himms-Hagen has looked at the skeletal muscle mitochondria during cold-acclimation and has found no evidence of a change in the efficiency of those organelles. The physiological basis of their enhanced response to catecholamines remains an open question, she says.

The search for the basis of nonshivering thermogenesis, which supplies warmth to a rodent digging in the snow, a bat coming out of hibernation and a newborn harp seal pup, continues in many laboratories in many countries. □