

THERMOBIOLOGY

Edited by

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1967



ACADEMIC PRESS · LONDON and NEW YORK

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U.S. Edition published by

ACADEMIC PRESS INC.

111 FIFTH AVENUE

NEW YORK, NEW YORK 10003

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Library of Congress Catalog Card Number: 67-18163

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Chapter 12

Resistance to Cold in Mammals

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I. Foundations

It is customary to name the maintenance of deep body temperature "homeothermy", while heterothermous (poikilothermous) animals are those in which deep body temperature follows the temperature of their environment. In a homeotherm, a regulated flow of *heat* determines body *temperature*. Hence the term "homeothermy" can mislead, since it may seem to mean "steady heat", instead of "steady temperature", and in this way perpetuate the confusion between heat and temperature which has bedevilled the growth of animal energetics. Mendelsohn (1964) shows how the subject remained undeveloped until the concepts of heat and temperature were separated. Heat as a quantity of energy, and temperature as a measure of the ratio of heat content to heat capacity, are rarely separated in general usage, and are still confused even in some scientific contexts.

The most convenient definition of a "homeotherm" is an animal which maintains a steady internal temperature in a wide range of external temperatures. A heterothermous animal, on the other hand, has a nearly constant temperature only in an environment which has itself an almost unvarying temperature.

General reviews of thermoregulation have been published by Hardy (1961), Thauer (1961), von Euler (1961) and Bligh (1966). Constancy of core temperature in a fluctuating environment demands regulated heat production and heat flow. A brief exposure to cold requires only a temporary increase in heat production or thermal insulation; the latter may be brought about by behaviour such as nest-making. Long-lasting exposure entails structural changes as well, as part of a chronic adaptation which can occur only if there is plenty of food. Usually, if the thermal demand of the environment (Burton and Edholm, 1955) for long exceeds the temperature-maintaining ability of the organism, the animal dies. But there are part-time homeotherms, such as the humming-birds, Trochilidae (Lasiewski, 1963), which develop a regular nocturnal hypothermia; this is an energy-saving process in animals that need a high metabolic rate to maintain their body temperature. Similarly, seasonal hibernation, with its accompanying hypothermia, is a means of evading the consequences of food shortage in winter.

These special cases excepted, the outcome of a homeotherm's struggle against cold depends on the relation between three quantities: heat production, thermal insulation, and the temperature difference between the animal's core and the environment. The three main sorts of outcome of exposure to cold—metabolic, insulative (Hart, 1963,

1964a,b), and hypothermic (Hammel, 1964)—reflect these primary factors.

II. Heat Production and Loss

A. THERMAL NEUTRALITY

The basal metabolic rate is conventionally defined as the metabolic rate of an animal (a) resting, (b) post-absorptive, (c) in a thermally neutral environment; but this concept has some defects. Giaja (1938) points out that, to obtain a "true" basal metabolic rate, the animal should first be for a time in an environment which does not call for any change in heat production. However, ignoring such refinements, a resting rate can be determined, for many species, of about 40 kcal./hr. m.² body surface.

A thermally neutral environment, then, is one in which an animal produces heat at the minimum rate. When the environment cools, a point comes at which the metabolic rate begins to rise; this is the *critical temperature*. The lower the critical temperature, the greater is the possible economy in energy expenditure. In some arctic species, this is realized to a remarkable degree. An extreme is the very low critical temperature of -40° in the arctic fox, *Alopex lagopus* (Scholander *et al.*, 1950); this is due to a thick coat of hair.

Heavy insulation makes it difficult to dissipate heat arising from activity. Yet the arctic fox, despite its thick fur, can run for long periods without pause. In general, heat can be lost by radiation and convection (and, to a small degree, by conduction), and by evaporation (reviewed by Mount, 1966a). The non-evaporative heat loss from a heavily coated animal is small, and takes place mainly from the poorly insulated head and legs (Irving *et al.*, 1955; and see Section II.B. 5). An Eskimo dog, *Canis*, does not melt snow on which it lies down to sleep (Hammel, 1964). But evaporative heat loss can be increased considerably through panting (Hardy, 1955), and such loss is independent of temperature gradients or thermal insulation. Some of the extra heat produced during activity may be dissipated in this way.

In a resting mammal at thermal neutrality, body temperature is maintained mainly by control of the circulation in the skin, and by sweating—the so-called "physical thermoregulation". As the temperature rises, heat is lost increasingly by sweating or, in animals such as the pig (Mount, 1963a; Ingram, 1964a) and sheep (Brockway *et al.*, 1965) which sweat little, by increased respiratory movements. A further rise in ambient temperature produces a rise in body temperature. The fully fleeced sheep, with a respiration rate of 90–120/min. at 20° ambient temperature, seems often to be near this point. After shearing, the rate falls to 16–20/min. (Bligh, 1963), a rate more usual for a mammal of this

size. However, if the metabolic rate does not rise above the minimum characteristic of thermal neutrality, the animal is by definition still within that zone, in spite of the work being done by thermoregulatory mechanisms.

Peripheral vasoconstriction also contributes to insulation. It does not, however, always coincide with a rise in metabolic rate. The metabolic rate of fat men in a water bath rises when the bath temperature is lowered below 33°, although the maximum tissue insulation is not

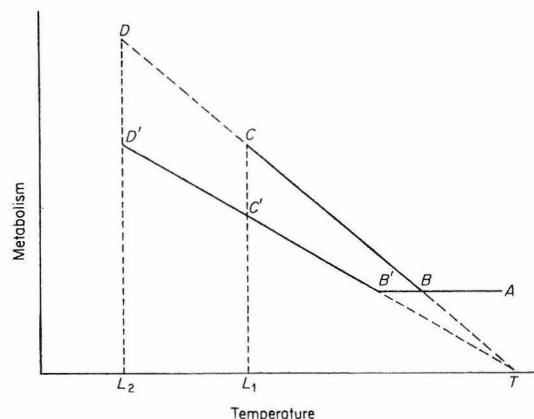


FIG. 1. A diagram of the relationship between an animal's metabolic rate and the ambient temperature. As the animal's insulation increases, the slope moves from BC to $B'C'$, pivoting on the animal's deep body temperature, T . The critical temperature falls at the same time from that opposite B to B' , and the cold limit falls from L_1 to L_2 , at the same maximum metabolism; this is insulative adaptation to cold. In "metabolic" adaptation, the curve BC is extended to BCD ; at this point, the cold limit is extended from L_1 to L_2 by a rise in metabolic rate from $C = D'$ to D . Variation in the level of minimal metabolism A , would move B relative to the temperature scale, and thus change the critical temperature. (After Hart, 1964a)

achieved until the temperature is much lower (Cannon and Keatinge, 1960). Since the metabolic and vasomotor responses do not occur at the same water temperature, these authors suggest calling the first the "metabolic threshold temperature"; they calculate a "theoretical critical temperature", that is, the lowest water temperature in which a man could in theory achieve thermal stability without an increase in metabolic rate. It is, however, probably better to give two critical temperatures, based on metabolic rate and skin circulation, respectively. For thin men, these temperatures are not far apart; and the same applies to another bare-skinned mammal, the young pig (Mount, 1959, 1964a).

The reciprocal of the insulation conferred by superficial tissues, that is, the thermal conductance, is proportional to the skin blood flow (Hensel, 1956). In a bare-skinned mammal (man: Miller and Blyth, 1958; pig: Irving, 1956; Mount, 1963b) subcutaneous fat enhances the control of insulation achieved by changes of peripheral blood flow. When the blood vessels of the skin are dilated, the subcutaneous fat can have little effect, since warm blood is moving through it to the surface, where heat exchange with the surroundings can take place. After vasoconstriction, this shunt no longer exists, and heat exchange must then take place through the fat. In the new-born pig, which has no subcutaneous fat but in which peripheral vasoconstriction does occur in the cold, the effect of vasomotor control on tissue insulation is relatively small (Mount, 1964a). In the older pig, which has subcutaneous fat, the effect is much greater (Ingram, 1964b). Vasomotor changes in animals with thick hair are probably less significant: little of the skin is in direct contact with the environment; hence skin temperature is closer to that of the core (Bligh, 1963).

While the white fox has a very low critical temperature, bare-skinned mammals such as naked man (Burton and Edholm, 1955), the young pig (Mount, 1960) and the shorn sheep (Graham *et al.*, 1959) have high critical temperatures. Hence critical temperature, thermal insulation and deep body temperature are intimately related (Fig. 1).

B. HEAT FLOW AND ENVIRONMENT

1. Modes of Cold Adaptation

When a mammal is exposed to cold, there are usually changes both in heat production and in insulation. Sometimes the response is almost wholly either one or the other. The effect on laboratory rats, of exposure to cold in the laboratory, is a rise in metabolic rate; but wild rats, exposed to the more complex situation of winter out of doors, also improve their insulation (Héroux, 1962). In a discussion on differences of insulation between individuals, Kleiber (1947) quotes an experiment carried out by Hoesslin in 1888. Hoesslin reared two dogs from the same litter, one at 32° and the other at 5°. Kleiber points out that the animal in the cold had to cope with a temperature difference between body and environment six times as great as that to which the other dog was exposed; yet the cold-exposed dog's metabolic rate was only 12% higher. The cold-exposed dog's hair, however, weighed three times that of its litter mate.

This is an example of chronic adaptation to cold. The acute response to cold must always be primarily metabolic. Even in the acute case, however, an insulative component enters in the form of changes in

posture, pilo-erection and, if exposure to thermal neutrality preceded the cold, peripheral vasoconstriction as well.

2. Heat Flow

Heat flow from an animal to its environment obeys Fourier's law, which states that heat flow between two regions is proportional to the temperature difference and to the thermal conductance (Kleiber, 1961). Kleiber disagrees with the commonly held view that heat loss takes place according to Newton's law of cooling, which states that the rate of cooling is proportional to the temperature difference between the body's surface and the surroundings. He points out that, since the body's temperature is regulated, a simple law of cooling does not apply. In practice, the difference between these laws is not great; but when, for example, thermal insulation is changing, Fourier's law is superior, since it deals with a regulated flow rather than one which is diminishing as the body cools.

3. Maximum Metabolic Rate

In theory, the limit of thermoregulation in the cold is set by the animal's maximum metabolic rate. In practice, such high levels of heat production, which can be kept up for short periods on sudden exposure, have little relevance to cold resistance, because the animal cannot maintain them.

This situation has been examined in young pigs in the first week after birth (Mount, 1961, 1963c). A new-born pig weighs rather more than 1 kg. at birth and is unusually mature. It has little thermal insulation; subcutaneous fat is absent, and there is little hair. The animal's defence against cold must therefore be primarily metabolic (Mount, 1959); but it may also be helped by postural changes, huddling with its litter-mates (Mount, 1960, 1964b), and by nesting material.

The metabolic rate of pigs less than 1 week old approaches a maximum at about 5° environmental temperature at low air movement (10 cm./sec.). In these conditions, the highest rate observed in any pig was 162 kcal./m.²hr.; the mean maximum for 31 pigs was 133 kcal./m.²hr. (Mount, 1963c). About half the animals managed to maintain their body temperatures, by means of a high metabolic rate, when they were kept at 5° singly for up to 6 hours. The temperatures of the others fell progressively.

The reciprocal of the rate of fall of rectal temperature gives a measure of the thermoregulatory capacity or cold resistance, in terms of the time taken for body temperature to fall 1°. The longer this time, the greater is the animal's cold resistance. Only about two-thirds of the variance of this estimate of cold resistance in young pigs can be accounted for by

variation in age and body weight. The correlation of rectal temperature change with cold resistance increases markedly if the individual "metabolic capability" is taken into account (L. E. Mount, unpublished observations). Metabolic capability is estimated as the metabolic rate when the rectal temperature is 36° and falling. It is argued that, when the rectal temperature is falling, the animal's metabolic rate is at the maximum, since added to the metabolic stimulus provided by a low environmental temperature is the effect of a falling deep body temperature (Mount, 1961). The pig's normal deep body temperature is close to 39°; when it has fallen to 36°, owing to cold exposure, the metabolic rate is held to be the maximum for that deep body temperature, *and to be limited by that temperature*. This is an important consideration for the comparison of maximum metabolic rates between animals, either of the same or of different species.

When the deep body temperature of a young pig begins to fall below about 37°, the metabolic rate has passed its maximum and is beginning to decline. As the body temperature falls still further, the decline follows a slope corresponding to a Q_{10} value of about 2. A similar Q_{10} value was found by Graham *et al.* (1959) in mature sheep above thermal neutrality. But often a considerable change of body temperature entails little change in metabolic rate. Adamsons *et al.* (1965) found similar metabolic rates in new-born human babies with deep body temperatures from 33.5° to 37.5°. This could be related to the incomplete development of the thermoregulatory mechanisms at birth less complete than in the pig.

A Q_{10} value for the whole animal might hold only at minimum or maximum metabolic rates; at intermediate rates, no simple correlation would be expected between metabolic rate and body temperature, since regulatory mechanisms alter the relationship. At minimum and maximum rates, however, there is no regulation. Young pigs at 4° have a mean Q_{10} value of about 2.9, with 95% confidence limits of 1.5 to 5.3; at 30° the Q_{10} value is 4.8, with limits 2.4 to 9.7 (Mount and Rowell, 1960). The critical temperature for these pigs is about 34° (Mount, 1959); hence the metabolic rate is regulated at 30°; at 4° the rate approaches the maximum, and therefore unregulated, level.

The observations of Silverman and Agate (1964), on small new-born human infants, are in accordance with those on pigs: the body temperatures of all infants fall in air temperatures controlled at 32° and 34°. Some infants prevent a marked fall in deep body temperature by increasing oxygen consumption, but others do not. Evidently there is considerable variation in metabolic capability, as in pigs.

The human baby and the piglet are good subjects for the investigation of cold resistance, since they have such low thermal insulation. Mature

mammals have a subcutaneous layer of fat, a capacity for peripheral vasoconstriction and, in some species, a highly insulating coat. Even pigs have considerable thermal insulation, when resident in the Arctic (Irving, 1956). The other important feature of a mature mammal is that the cold must be intense before it induces a maximum metabolic rate. Iampietro *et al.* (1960) managed to achieve high rates in naked men by the use of wind in a cold environment. In a coated species, Alexander (1962) achieved maximum rates for lambs in an apparatus in which he could not only lower the temperature but also produce a wind and wet the animal as well. The cold had to be more severe than for young pigs, since a lamb's thermal insulation is about twice that of a piglet. The rectal temperature was made to fall at about $3^{\circ}/\text{hr.}$, and oxygen consumption was then measured for 20 min. Wet lambs in a wind produce heat at rates as high as $250 \text{ kcal./m.}^2\text{hr.}$, compared with the piglet's upper limit of $162 \text{ kcal./m.}^2\text{hr.}$ The higher metabolic capacity and higher thermal insulation of lambs allow them to tolerate about three times the cold stress which can be withstood by young pigs. This is matched by the considerably greater cooling to which the lamb is exposed in its usual outdoor habitat, as compared with the young pig which, in natural conditions, lives in a nest with its litter-mates and the sow.

4. Metabolic Body Size

The "summit" or maximum metabolism of lambs is roughly proportional to body weight (Alexander, 1962). In this case the rectal temperature has no effect. In the young pig, however, there are clear effects of rectal temperature on the metabolic rate measured at 4° , that is, near the animal's cold limit (Mount and Rowell, 1960). When the effect of rectal temperature has been allowed for, metabolic rate is proportional to body weight raised to the power 0.56. The figure of 0.56 is not significantly different from the 0.67 power corresponding to the so-called "surface law". Alexander's value of 1.0 is, on the other hand, significantly different from 0.67. For maximum metabolism, Alexander's figure for lambs is a more probable one than that of Mount and Rowell for pigs, since an exponent of body weight of 1.0 means that the maximum metabolism is proportional to the active body mass, assuming that all the animals have similar body compositions.

The same reasoning may be applied to the reference base for the minimum metabolic rate at thermal neutrality. The standard metabolism of normal human infants between eight days and one year is proportional to body weight (Karlberg, 1952). In older infants and children, however, the relationship is closer to the 0.75 power of the body weight used for comparisons between species (Kleiber, 1947). Karlberg suggests that the higher exponent in infancy is due partly to

the influence of growth on energy metabolism. At minimum or maximum metabolic rates, the heat production of mature animals may be proportional to active body mass. Between these limits, proportionality is likely to be some function of body size which takes into account the areas, shapes and insulation of all the parts of the organism.

This relationship between metabolic rate and body structure has been called the "metabolic body size" (Kleiber, 1947). Some workers have denied that there is any unifying type of function which could apply to different species. Benedict (1938) considered it futile to try to find one. However, as Kleiber has pointed out, a large animal produces more heat per unit time than a small animal, and a basis for comparing animals of different sizes is a rational objective. Many measurements of the metabolic rates of different species have been made. They show that the metabolic rate of both large and small homeotherms is more nearly proportional to body surface area than to body weight (Kleiber, 1947).

This is the basis of the "surface law", first postulated in 1839. It was held that an animal's heat production was proportional to its surface area, and hence for animals of the same shape and density it must be proportional to the 0.67 power of the body weight. Surface area, calculated from various equations, has been used in a great deal of metabolic work. However, several authors, notably Brody (1945) and Kleiber (1947), have been concerned rather with that function of body weight which has the most general application to metabolic rate.

For the equation $H = aW^b$, where H = rate of heat production, W = body weight, and a and b are constants, Brody eventually settled on the value of 0.70 for the body weight exponent, b . Kleiber determined the value of b as 0.75, and recommended this power of body weight as representative of metabolic body size. In standard conditions, he found that the metabolic rate of adult homeotherms, from mice to cattle, averaged $70 \text{ kcal./kg.}^{0.75} \text{ day.}$ To determine whether the metabolic rate was proportional to W or to $W^{0.75}$, it was necessary that the heaviest animals weighed at least three times as much as the lightest. This was a consequence of the great variation in the figures used. Similarly, the 0.67 and 0.75 powers could not be distinguished unless there was a nine-fold weight range.

A fixed value of the exponent is useful only in a given set of conditions—for example, with standard metabolism in mature animals. Mount and Rowell (1960) give an analysis of the variance of metabolic rate for pigs in relation to age, body weight and rectal temperature. The effect of age is not significant during the first week, but the effect of rectal temperature is significant. The exponent of body weight which gives proportionality to metabolic rate is 0.86 ± 0.05 at 4° and 30° ambient temperatures, when the effects of age and rectal temperature

are ignored, but 0.60 ± 0.06 when age and rectal temperature are allowed for. This represents a considerable difference.

The same problem has recently been considered by Gridgeman and Héroux (1965) in relation to measurements of oxygen consumption in rats. They show that the body weight exponent can be an unstable parameter, although they have no ground for opposing Kleiber's (1947) recommendation of the use of the 0.75 power for homeotherms in normal conditions. They find, however, that the exponent can be influenced by exceptional conditions, particularly of temperature. Their general recommendation is to use analysis of covariance to allow for the effect of body weight on oxygen uptake, and so derive experiment-specific values of the exponent. This involves no assumptions about the exponent, and allows for ancillary factors which may vary from experiment to experiment.

5. Insulation

Body temperature in cold conditions is maintained most economically, that is, with the lowest heat production, when the insulation is high. The effective insulation is, however, not a simple, unvarying quantity. It most closely approaches fixity in an animal such as the arctic fox, in which the very high insulation of the coat determines the non-evaporative heat loss. The same is true for the fully fleeced sheep. More usually, however, the coat is only one component of insulation, and may itself change by pilo-erection and as a result of penetration by wind.

The factors which determine the efficiency of insulation may be divided into two groups: (i) those which affect the insulation per unit area of the animal's surface, that is, the specific insulation (Kleiber, 1947), and (ii) those which affect the total insulation.

a. Specific insulation. The effects due to peripheral vasoconstriction and subcutaneous fat have already been discussed (Section II.A, p. 413). The hair or wool coat, when it is present, however, is the major factor in specific insulation. The presence of a coat has a clear effect on the skin-air temperature gradient. The thermal impedance which it offers depends on the air trapped between the fibres: a smoothed coat offers less insulation than the same coat with hairs raised and a thicker layer of air. Blaxter and Wainman (1961) conclude that in steers pilo-erection is responsible for a large part of the difference in measured insulation above and below the critical temperature.

The density of the hair fibres is also important. Berry and Shanklin (1961) used a heat-flow meter applied to the coat surface to measure the total hair-coat insulation of dairy calves. The insulation was linearly related to the hair weight per unit area of body surface. Mount (1964a) recorded the metabolic rates of shaved and unshaved new-born piglets,

and so estimated the insulation conferred by their sparse hair coats. He found a total hair insulation of $0.03^{\circ}\text{m}^2\text{hr./kcal}$. The corresponding figure for the calf is $0.08^{\circ}\text{m}^2\text{hr./kcal}$. The hair density of a calf is about 9.8 mg./cm^2 , however, and that of a piglet only 1.5 mg./cm^2 . For a given amount of hair, therefore, a pig's hair insulation is about 2.5 times greater than that of a calf's. Hence, although Berry and Shanklin (1961) find a linear relation between hair density and degree of insulation among calves, this relation does not necessarily extend to comparisons between species. Barnett (1959) measured the thermal insulation of excised mouse skin, shaved and unshaved. From his figures, it is possible to calculate, with certain assumptions, that the hair density of the mouse skin is about 0.6 mg./cm^2 , and that at a density of 1 mg./cm^2 the thermal insulation is $0.08^{\circ}\text{m}^2\text{hr./kcal}$. At the same hair densities, this is about four times the insulation of pig hair, and ten times that of calf hair. Hence mouse coat, per unit weight, is better than either pig or calf hair. This may be because a great density of fine hairs provides a better trap for still air.

Blaxter *et al.* (1959) made a study of the insulation offered by the fleece of the sheep. Values derived from measurements on excised pelts may, however, not apply in the living animal. The growth of wool increases the area available for heat exchange; it allows spreading of fibres at the periphery and so permits greater heat loss by convection; and it leads to "cracking" of the fleece, that is, the appearance of divisions in the fleece as the sheep moves its body. However, fleece does not cover the whole of the sheep. When allowance is made for this by including estimates of the areas not covered, *in vivo* estimates of fleece insulation do not differ greatly from those determined on excised pelts. The insulation of fleece and hair falls within the range $0.16\text{--}0.20^{\circ}\text{m}^2\text{hr./kcal}$ per cm. length of coat.

The penetration of fleece by wind decreases the thermal insulation of the coat (Joyce and Blaxter, 1964). In sheep with different fleece lengths, impairment of coat insulation is detectable over the whole range of wind speeds from 27 to 430 cm./sec. At 430 cm./sec., it is 42%. It can be calculated that, at 430 cm./sec., a closely clipped sheep loses 55% of the insulation that it possesses in a wind speed of 27 cm./sec. The corresponding loss for a sheep with a 30 mm. fleece length is 44%, but the fleeced animal has a much higher insulation initially. The figures indicate the greater susceptibility of the bare-skinned mammal (in this case the closely clipped sheep) to increments of wind speed, compared with the coated animal. Even so, the influence of wind speed on a new-born pig is less than that on a stationary, heated model, perhaps owing to the effects of posture (Mount, 1966b).

b. Total insulation. The total thermal insulation may be defined as the

ratio of the body-environment temperature difference to the total non-evaporative heat flow. Although a heavy coat may be a dominant component of a mammal's insulation, no one component determines by itself the total non-evaporative heat loss. In the resting animal this is shown by the effect of postural changes on heat flow (Benzinger and Kitzinger, 1963). Lowering the ambient temperature leads a young pig to decrease its effective radiating surface area; but it probably increases the convective heat loss by inducing shivering (Mount, 1964b). Grouping animals together (Kleiber, 1961; Mount, 1960) or providing nesting material (Sørensen, 1962) decreases heat loss. When animals move about and leave the group, heat loss increases considerably. An active animal exposes an increased body surface area and increases air movement over its surface; hence there is a rise in metabolic rate from this cause, as well as that resulting from muscular action.

The rate of cooling of a body in air is proportional to its surface area, that is, to $W^{0.67}$, if other conditions remain constant; and it is inversely proportional to the heat capacity, that is to W , if the mean specific heat remains constant. Combining these effects, the cooling of a given body is then proportional to $W^{-0.33}$ (Kleiber, 1961); the larger the body, the more slowly it cools. For an animal of 1 kg. body weight, $W^{-0.33}$ is 1; for 8 kg., it is 0.5; for 27 kg., 0.33, and so on. By the same reasoning, the heat input, required *per unit body weight* to maintain the body temperature, falls progressively as body size increases. This is a reflection of the "surface law" discussed earlier, and shows how the thermal insulation of an animal rises simply as body size increases; no change in the specific insulation is required to bring about the rise. Usually, animals grow, and also increase their specific insulation by coat and subcutaneous fat, at the same time, so that the cold tolerance of older and larger animals is increased out of proportion to the increase in size. Another effect of size depends on the radius of curvature of parts of the animal: fingers lose more heat, both per unit area and also per unit of temperature gradient, than does the trunk (Hardy, 1949). The disposition of limbs in relation to the body, the control of posture, and the proportion of time in which the animal is active and therefore exposing more of its appendages, have a marked effect on the total thermal insulation and therefore on cold resistance.

Hart (1964a) refers to the presence of thinly furred tissues in the appendages of heavily insulated mammals as solving the problem of exercise heat on the one hand, and conserving heat by cooling on the other. There is considerable variation in skin temperature in the appendages; this is in contrast to the skin under thick fur, which remains uniformly warm. Hart points out that the cooling of peripheral tissues has an insulating effect. This is accompanied by a remark-

able ability to withstand changes of temperature, and by the presence of structures which allow alterations in the rate of heat loss.

Heat exchange in homeotherms has also been discussed by Scholander (1958). Mammals in the cold are protected from heat loss largely by their fur, yet the legs and other appendages of arctic mammals are poorly insulated, and seals, for example, swim about in very cold water with hairless flippers. If these appendages were kept warm, the heat loss would be very great. In fact, they are at rather low temperatures, and it is by a remarkable degree of local cold adaptation that the tissues maintain normal function and irritability. Other tissues do not function at these temperatures. Hart (1964a) refers to the ability of peripheral nerves in the legs of cold-adapted gulls to conduct at lower temperatures, and to cell division in the peripheral tissues of cold-adapted rats. Cell division in the peripheral tissues, however, occurs only in animals that have been exposed to cold for some days (Héroux, 1959a). It depends on the resumption of a normal blood supply to the skin; this in turn requires a substantial increase in the rate of heat production (discussed below in Section II.C, p. 424).

Scholander (1958) discusses the way in which the extremities of cold-adapted mammals are held at a low temperature. Heat from arterial blood is shunted back into the veins before the blood reaches the periphery. The testicle of most mammals is provided with a counter-current vascular system, and this no doubt contributes to keeping it at a temperature lower than that of the body core (Waites and Moule, 1961). A simpler form of thermal shunting may regulate heat dissipation, in exercise and rest, from the poorly insulated limbs of the arctic fox. In man, the temperature in the brachial artery can fall by as much as $0.3^{\circ}\text{C}/\text{cm}$. through transmission of heat to the veins (Bazett *et al.*, 1948). Scholander considers this simple system to be rudimentary compared with the multichannel arteriovenous rete systems (networks of blood vessels) which have been described in the manatee (*Manatus*), whales (Cetacea), and tall wading birds, among others. The retes are usually at the bases of limbs, tail or fins. They probably not only aid in conserving heat, but also contribute to heat loss. Heat loss, rather than conservation, is evidently a main function of the hairless tail and feet of rats (Thompson and Stevenson, 1965) and presumably of other Muridae.

6. The Effective Environment

The metabolic effort required to maintain body temperature is not a simple function of air temperature alone. Although lowering the air temperature raises the metabolic rates of exposed men, the highest rate is observed in a wind at an air temperature higher than the lowest a man can stand (Iampietro *et al.*, 1960).

The "thermal demand of the environment" is the total heat loss through radiation, convection and conduction (Burton and Edholm, 1955). In cold conditions, evaporative heat loss continues, mainly from the respiratory tract, but it is relatively slight. Air movement and radiant temperature have a marked influence on heat loss. Air at 20°, moving at 30 cm./sec., produces greater heat loss from the backs of pigs than nearly still air at 15° (Mount and Ingram, 1965). Thirty cm./sec. is not a high air speed, but it is equivalent in this case to a 5° difference in ambient temperature. For lightly dressed persons, the subjective effect of an increase in air temperature of 1° can be nullified by a decrease of 1.39° in the mean radiant temperature (Koch, 1962). Determinations of heat loss in new-born pigs have shown similar effects of air and radiant temperatures on metabolic rate (Mount, 1964b, 1965).

There have been many attempts to find a way to express in a single term the effects of the environment on an animal's heat loss. Yaglou (1949) came to the conclusion that such a concept was unrealistic, and that it was necessary to make separate estimates of heat exchange through the four channels of radiation, convection, conduction and evaporation; a unitary estimate would not be useful for different subjects under different conditions. Burton and Edholm (1955) have examined the "equivalent still air temperature" as applied to man, and have shown how a thermal wind decrement and a radiation increment may be calculated in the form of temperature differences to be added algebraically to the air temperature to give the "still shade temperature". Although these calculations are suitable for man in specified conditions, they do not necessarily apply to other mammals (Mount, 1965).

To sum up, the effective environment comprises a number of factors, the combined effects of which cannot be stated for all mammals by any single universally applicable quantity. The influence of each factor must be assessed separately.

C. PHYSIOLOGICAL ADAPTATION TO COLD

1. Metabolic Rate

The most important recent contributions to the study of metabolic rate in cold adaptation have been on "non-shivering thermogenesis". When a mammal is first exposed to cold, if the cold is severe enough the animal shivers and so produces more heat. The blood supply to the periphery is also decreased. After some days the shivering and peripheral vasoconstriction decline, but heat production remains high. This sequence is well substantiated in laboratory animals (Cottle and Carlson, 1956; Davis *et al.*, 1960); it has also been recorded in wild animals, for

instance by Pohl and Hart (1965) in a ground squirrel, *Citellus tridecemlineatus*; and it has been demonstrated in man (Davis *et al.*, 1959). The important sites of non-shivering heat production are not yet fully known, but evidently include the viscera and still more the skeletal muscles and brown adipose tissue (Smith, 1964; and see Section VII.A). In cold-adapted animals, noradrenalin stimulates thermogenesis (Leduc, 1961). Men living in a cold environment are more sensitive to noradrenalin (Joy, 1963), and this is indirect evidence for cold adaptation in man. The same applies to rats (Héroux, 1963).

The experiments of Scholander and his colleagues (1958a) on the effects on man of exposure to cold also illustrate the "metabolic" type of adaptation to cold in man. Eight young men lived for 6 weeks in the autumn in primitive conditions in the Norwegian mountains. They wore only light summer clothing during the day, and took exercise by hiking and hunting. Each slept in a simple wind-proof blanket bag under a shelter open on one side, at an air temperature of about 4°. The oxygen consumption of these men was higher than that of controls; their skin temperatures too tended to be higher. They resemble those of the thinly clad Alacaluf of Tierra del Fuego (Hammel, 1964). Hammel points out that the response of these men to moderate cold represents a clear example of metabolic adaptation, and that Arctic Indians and Eskimo behave in a similar way.

2. Enzymic Changes

The extra "non-shivering" heat produced by a cold-adapted homeotherm is an index of intracellular changes in catabolism. This large subject has been reviewed, with full bibliographies, by Sellers (1957), Depocas (1961), Smith and Hoijer (1962) and Hannon (1963). As Depocas (1961) remarks, thermoregulation provides a convenient means of studying the control of the release of energy.

It might be expected that, once shivering had ceased, it would be possible to detect a changed but stable pattern of enzymic activity in, for instance, the liver of a cold-adapted animal. This is not the case. Substantial changes continue, even between 30 and 150 days of exposure, in the livers of laboratory rats kept at 4° (Fig. 2). Hence, even in this one situation, there are evidently at least two phases of cold adaptation without shivering. For this, as for other aspects of adaptation to cold, the precise conditions of experiment, especially the duration of exposure, must be clearly specified. This requirement is illustrated, not only by changes in enzyme activity, but also by the rates of oxygen consumption of liver slices *in vitro* (summarized by Smith and Hoijer, 1962). The rate of oxygen uptake rises during the first 30 days of cold

exposure, but after this it declines; by about 120 days there may be no decisive difference from the control figure. Yet, in some experiments, the rate of oxygen uptake by the whole animal remains indefinitely more than 2.5 times that of controls at about 23°. The discrepancy may be related to the enlargement of the liver and other heat-producing tissues (discussed below in Section V, p. 442), partly to a belated increase in heat production by other organs, especially muscles; or changes in the intact animal may not be fully reflected in the metabolism of isolated tissues. A quantitative expression of all these effects is needed, but is not yet available, even for laboratory rats.

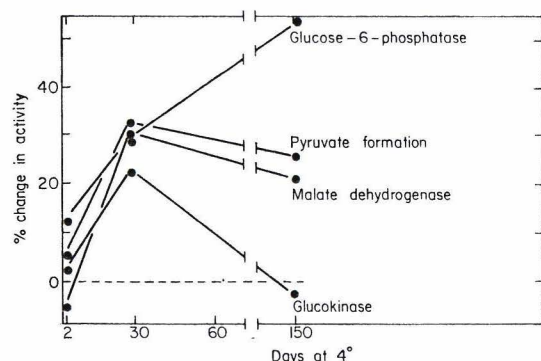


FIG. 2. Activity of liver enzymes during exposure of laboratory rats to cold. (After Hannon, 1963)

Specific changes in enzyme activity have been reviewed especially by Hannon (1963). Most of the scattered information concerns carbohydrate metabolism. After two days at 4°, the activity of liver lactate dehydrogenase, measured by lactate formation, has risen by about 50%. This is only a temporary phenomenon, possibly related to the increased heat production by shivering. After thirty days' exposure, lactate dehydrogenase activity is back to normal, but other changes in enzyme activity have become evident.

The activity of glucokinase, which catalyses the phosphorylation of glucose, is increased by 20%. The activity of other enzymes involved in the Embden-Meyerhof pathway is also increased; these include phosphoglyceromutase, phosphopyruvate hydratase (enolase), and pyruvate kinase. Hence the rate of formation in the liver of pyruvate from dietary glucose is evidently increased at this stage of cold adaptation. At the same time, the activity of liver dehydrogenases that catalyse reactions involved in the tricarboxylic acid cycle is increased.

A special case, evidently, is that of glucose-6-phosphatase (Fig. 2). The activity of this enzyme, measured by phosphate formation, increases in the liver during the first days of cold exposure, and by thirty days is raised by about 35%. But the increase continues even after thirty days. This enzyme is involved in the reversed Embden-Meyerhof pathway. Its increased activity may signify a greater rate of gluconeogenesis.

These observations concern the use of dietary carbohydrate as the source of energy. As for alternative sources, a few facts bear on the use of protein. During only two days' cold exposure, the activity of liver (and muscle) transaminases rises, and the new level is evidently maintained for many weeks. Hence, it is supposed, the rate at which amino acids can be used for heat production is increased. This is accompanied by a temporary cessation of growth or even by a loss of body weight (Fig. 5, p. 436). This topic, and observations on fat metabolism, are discussed in Section V, p. 442.

3. Endocrine Changes

Until recently, nothing could be said about the intracellular enzymic changes described above, but the endocrine adjustments during cold exposure have been known for decades. Hormones are now seen as the agents which provoke the cellular changes. Lowered temperature of the skin and colon induce not only shivering but also, by way of the hypothalamus, increased secretions of pituitary and other hormones (Hsieh *et al.*, 1957; von Euler and Söderberg, 1958; Anderson *et al.*, 1963; Benzinger, 1964).

On exposure to cold there is an immediate increase in the secretion of catecholamines by the adrenal medulla. Of these, noradrenalin is especially important. This hormone activates liver phosphorylase reactions, and so increases the rate of production of glucose 1-phosphate from glycogen. This is evidently part of a mechanism for the prompt mobilization of reserves of energy. Noradrenalin probably continues to play an important part in cold-adapted animals, for—as we saw above—the responsiveness of the tissues of these animals to noradrenalin is increased (Carlson, 1960).

The response of the thyroid is less rapid. Brown-Grant (1956), for example, exposed laboratory rats to a temperature of 6–12°, and observed increased thyroid secretion within 8 hours. But more severe cold sometimes led to a decrease. Brown-Grant (1960), Keller (1960), Knigge (1960) and Anderson (1963) have discussed the control of thyroid secretion. The necessary part played by the pituitary has been demonstrated in several species. The increased secretion of thyroid-stimulating hormone (TSH) on exposure to cold depends in turn on the hypo-

thalamus: suitably placed injuries in the hypothalamus can result in diminished thyroid secretion, and electrical stimulation can increase it. If the pituitary stalk is cut, there is no thyroid response to cold. The action of thyroid hormone is usually said to be on catabolism: the effect of noradrenalin in increasing heat production is enhanced (e.g. Carlson, 1960; Smith, 1963). The role of thyroid hormone is, however, not simple. Fregly *et al.* (1961) confirm the importance of the thyroid for the survival of rats in severe cold, but show that cold can induce a rise in metabolic rate in the absence of the thyroid (cf. Hsieh and Carlson, 1957). But thyroidectomized rats lose heat at a greater rate than controls, evidently owing to loss of the ability to constrict peripheral blood vessels. The thyroid response to cold has also been observed in guinea-pigs, *Cavia*, (Yamada *et al.*, 1965): in them, too, it is necessary for the acute phase of cold adaptation.

Finally, there are the steroid hormones of the adrenal cortex. Since adrenocorticotrophin (ACTH) secretion by the pituitary increases immediately on exposure to cold, so also does the secretion of adrenal cortical hormones. The little relevant information on the action of these hormones is reviewed by Smith and Hoijer (1962). At least in adaptation to cold, their most important function probably concerns protein metabolism. The breakdown of keto acids for oxidation is accelerated by them. This is evidently a temporary measure to meet the demands for extra energy before food intake has increased. There is, however, even in a cold-adapted animal, a rise in protein turnover of the order of 50%. The additional deamination in the liver probably depends in part on the activation of enzymes. The breakdown of arginine to urea is evidently similarly regulated by adrenal steroids.

The recent rapid developments in knowledge of the chemistry of release of energy in cells, and its regulation by hormones, have made it possible to present in outline a causal chain from the first stimulus of cold to the final production of heat. Cold receptors, probably both peripheral and central, initiate reflex responses and also very rapid changes in the secretion of a number of hormones. The hormones in turn act on the cells which produce the extra energy. To what extent the various endocrine effects are confined to the period during which cold adaptation is taking place is not yet clear.

4. Insulation

Adaptation to cold, by increasing the metabolic rate, puts heavy demands on the food supply. Increasing thermal insulation, and hence the range of ambient temperatures which allow minimum metabolism, is a less hazardous mode of cold adaptation. Well known work on wild rats

(Héroux, 1959b; Héroux, 1962; Hart and Héroux, 1963; Héroux, 1963) has shown that the cold resistance of rats caught in the winter is superior to that of summer rats, and that this difference is related to the higher metabolic rates of which winter rats are capable. Winter rats tolerate ambient temperatures about 20° lower than summer rats. However, this metabolic adaptation is accompanied by changes in thermal insulation; winter rats have more fur and lower skin temperatures under the fur.

A larger species, the varying hare, *Lepus americanus*, has been studied by Hart *et al.* (1965). Animals caught in winter have 27% more hair than those caught in summer. Correspondingly, the critical temperature of winter hares is -5°, but that of summer hares is 10°. Evidently, in this species, seasonal adjustments are largely or wholly in insulation.

5. Hypothermia and Hibernation

The third group of ways in which homeotherms can adapt to cold involves lowering the body temperature. This decreases the level of metabolism required for a given degree of thermal insulation.

A distinction must be made between tolerance of environmental cooling, and tolerance of hypothermia. Tolerance of environmental cooling is achieved by increasing the metabolic rate or thermal insulation, or both, and so by maintaining deep body temperature. This may be accompanied by cooling of peripheral tissues, well demonstrated in pigs kept in arctic conditions (Irving, 1956). Tolerance of hypothermia, that is, a lowering of the body core temperature, does not necessarily accompany this. The two forms of tolerance do, however, go together in, for example, Australian aborigines (Scholander *et al.*, 1958b): these men undergo both a cooling of the body shell and a fall in deep body temperature during cold exposure at night, without an increase in metabolic rate. Europeans in similar circumstances feel cold, shiver violently and have a raised metabolic rate; they do not tolerate hypothermia.

As a rule, only when metabolic capacity is exceeded by the thermal demand of the environment does the animal succumb to an imposed and progressive hypothermia. In hibernating animals, by contrast, active thermoregulation is replaced by tolerance of hypothermia when the ambient temperature falls below a certain value. Hibernation has been reviewed by Kayser (1961) and Hoffman (1964). The heterothermic type of response, which occurs during hibernation, takes place only within a certain range of ambient temperatures: arousal occurs if the temperature falls below about -2° or above about 30°. Burton and Edholm (1955) quote the ground-hog's emergence from its burrow on or about 2 February ("ground-hog day") as a

probable example of the protective arousal which occurs when conditions become too cold. Soil temperature at burrow depth lags behind that of the surface, and is likely to reach its minimum at this time of year.

The metabolic rate during hibernation is about 1–3% of the basal value whilst awake. Basal heat production in summer varies directly with the surface area of the body, but during hibernation heat production varies with body weight (Kayser, 1959). These two “metabolic body sizes” may be related to the presence and absence, respectively, of nervous control. Kayser considers that thermoregulation of hibernators is deficient mainly through poor control of heat loss. When they are awake, their heat production, however, is higher in the cold than is that of other homeotherms, and their maximum metabolic rate during arousal by cold is higher than the peak reached during the summer.

Hoffman (1964) points out that, if they are not exposed to cold, animals which would otherwise hibernate behave as typical homeotherms. They do not prepare for hibernation until cold weather begins. For an animal with poor regulation of heat loss, hibernation is a means of solving the annual problem of food scarcity and other adversities.

III. Food Consumption

A. AMOUNT EATEN

Other things equal, to produce more heat an animal must eat more. The need for extra food, on exposure to cold, is especially marked in small mammals, owing to their high rate of heat loss from a relatively large body surface. Hence their food intake must be assumed to fluctuate with season, unless they hibernate. Campbell (1945) recorded a small rise, during several successive winters, even in laboratory rats, *Rattus norvegicus*, kept indoors. Stevenson and Rixon (1954) carried out more conventional experiments on laboratory rats: they exposed rats to 2–5°, and observed an increase in calorie intake, relative to body weight, of 40–50% over that in an ordinary laboratory temperature. Sellers *et al.* (1954) exposed albino rats to 1.5° for 6–7 weeks, and fed them on mixtures of constant protein content but with fat varying from 5 to 44% by weight. The raised calorie intake of the rats that survived was constant, at the low temperature, regardless of diet; growth was always less than at room temperature.

When a laboratory rat is transferred suddenly to a room at, say, 4°, it loses weight, much of it in the form of adipose tissue, as described below. Hence, during this initial phase, food consumption does not keep pace with heat production. However, laboratory rats

exposed to seasonal cold in groups do not lose weight; and healthy wild rats have more adipose tissue during winter (in Canada) than during summer (Héroux, 1963). This is evidence that a small mammal, unchanged by domestication, is able not only to eat and digest enough food in winter to maintain heat production, but can even “over-eat” and so increase the amount of its food reserves and possibly its insulation.

It has been supposed that large, well-insulated mammals do not have to eat more in winter, since they do not lose more heat in cold weather than in warm. This is evidently true for clothed man (Consolazio, 1963). The question has also been tested by Durrer and Hannon (1962) on domestic dogs, *Canis familiaris*. They kept five Alaskan husky dogs, each weighing 30–40 kg., out of doors in Alaska: in summer, their calorie intake was 49 kcal./kg.day but, by November, it was 87 kcal./kg.day, or 77% more, despite an extra growth of hair when cold weather began; body weight was, however, lower in winter than in summer (Fig. 3). In very cold weather, activity was much reduced: the dogs lay curled up, and were difficult to arouse; they got up to feed for only brief periods. Once the huskies were cold-adapted, more severe cold did not make them eat still more; but it did so in beagle dogs weighing 11–13 kg.

It is sometimes assumed that there is a simple, fixed relationship between the amount of food eaten, on the one hand, and heat production plus growth and storing of reserves, on the other. This relationship holds only if the efficiency of food utilization is constant. In some situations, an appearance of superior efficiency in a cold environment can be misleading. Andik *et al.* (1963) kept male laboratory rats at about 21°, and gave them a diet with only 4.3% protein. The rats stopped growing, and died within about 6 weeks. Other rats on this diet, kept at 5°, survived and grew; but return to the warm arrested growth and led to death in a few weeks. The primary effect of the cold environment was to double food intake. This incidentally increased the protein eaten to a level which permitted growth. Klain and Vaughan (1963), however, have described changes in enzyme activity in rats adapted to 7° for 3–4 weeks: these changes made possible growth on diets which, owing to an unbalanced amino acid content, did not support growth in rats kept in a warm environment. Here is authentic evidence of improved metabolic efficiency.

Work on inbred laboratory mice, too, has raised the question of food utilization, especially during pregnancy and lactation. Barnett and Little (1965) compared virgin, pregnant and lactating mice at 21° with similar mice at –3°. The latter had been born and reared in the cold environment; all mice had cotton wool nests. Relative to body weight, virgin mice ate about 70% more in the cold environment than in the

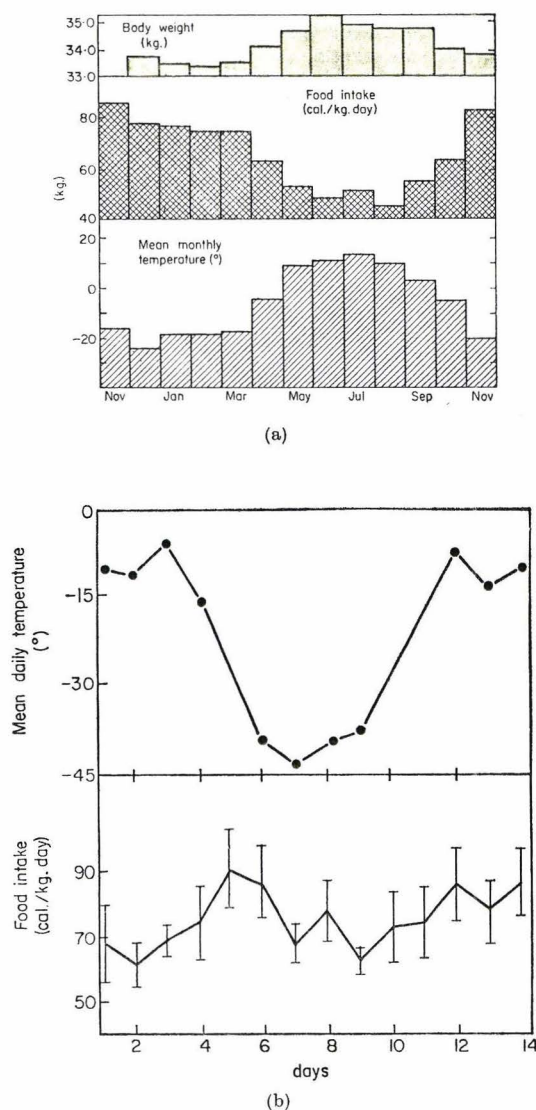


FIG. 3. Food intake and season in the dog, *Canis familiaris*. (a) Rise in food consumption of husky dogs in winter. Body weight falls. (b) Absence of correlation between food intake and brief fluctuations in external temperature (cf. Fig. 5). (After Durrer and Hannon, 1962)

warm, but the difference was less during pregnancy, and during lactation there was no difference (Fig. 4). Lactation is the most exacting test of a female's metabolism; probably, at this stage, food consumption was limited by the capacity of the gut (Barnett and Widdowson, 1965). Fewer young were born and reared at -3° than at 21° . The cost of rearing 10 g. of young to ten days, in terms of extra food consumed during the last 10 days of lactation, was about 18 g. at 21° but, in mice

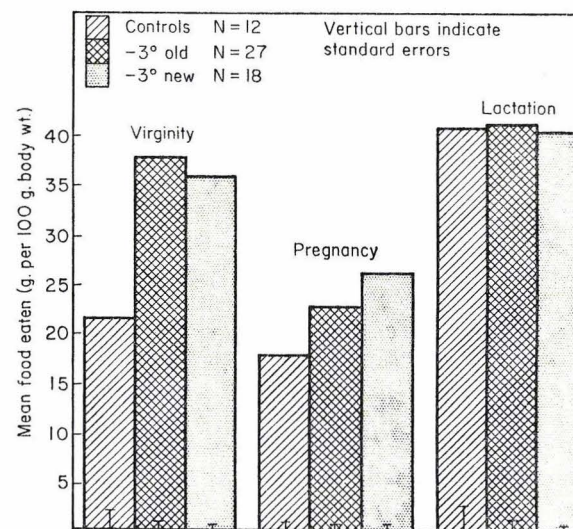


FIG. 4. Environmental temperature, and food consumption by female mice. The controls were kept at an ambient temperature of 21° . The new stock were first or second generations bred at -3° ; the old stock was of the 17th. to the 19th. generations at -3° . Virginity: mean daily weights of food eaten during the 9th. week after birth. Pregnancy: daily consumption during the last three days of pregnancy. Lactation: daily consumption during the first ten days after the birth of a litter. (After Barnett and Little, 1965)

of the same strain but of long ancestry in the cold, only 11 g. This suggests superior food utilization by the cold-adapted mice.

However, the ability of mice to breed in such a cold environment, on such a modest increase of food, probably depends partly on a decrease in the need for food through lowered activity, as we shall see later (Section IV.A, p. 437). Another means of reducing the need for food would be improved thermal insulation, but this cannot be an important factor for a small mammal (Section V.D.1, p. 449). Resort to a nest must, however, reduce heat loss (Section IV.B, p. 438). Probably,

time spent outside the nest is minimized in a cold environment, as Strecker (1955) observed in wild house mice, *Mus musculus*. Rapidly eaten meals at rather long intervals can promote a higher growth rate, and deposition of more tissue fat, than frequent meals, at least in laboratory rats (Cohn and Joseph, 1960; Hollifield and Parson, 1962a,b); hence, up to the limit imposed by the capacity of the gut, a "stuff and starve" regime may be no disadvantage.

B. COMPOSITION OF THE DIET

Studies have been made of the effects of varying the fat content of the diet on performance in a cold environment, but the results have been conflicting. Evidence in favour of a fatty diet comes from Dugal *et al.* (1945): the survival and growth of their rats, at -2° , was improved by a fat-rich diet. Pagé (1957) has reviewed work from his laboratory in which laboratory rats grew better when given extra fat; at room temperature the extra growth was due to formation of adipose tissue, but at 3° it was not. Giaja and Gelineo (1934) exposed rats to cold and fed them on protein, or fat, or carbohydrate alone. Judged by survival, a purely protein diet was little better than starvation; fat was less effective than carbohydrate. Similarly, Lang and Crab (1946) studied rats kept at 6° , on diets containing 10–50% of the calories as fat. The resistance of these rats to cold declined with increasing fat content of the diet. Bobek and Ginter (1966) too find that a diet high in fat and cholesterol retards the growth of rats exposed for 8 hr./day to 2° . The many factors, which might influence the ability of animals to use fat and other dietary components, preclude any confident explanation of the difference of the observations from those of Dugal, Pagé and their colleagues.

Another of the factors is again efficiency of food utilization. For example, Templeton and Ershoff (1949) found that addition of fat (margarine) to the diet reduced mortality due to cold only after the rats had undergone cold-adaptation by being exposed to 2° . Similarly, Pagé (1957) quotes work in which laboratory rats kept at 11° gained less weight than controls during their first month of exposure, owing to fat depletion; but, during the second month, there was a great increase in weight due to fat deposition. Such work shows that much information can be lost if experiments are restricted to only a few days or weeks.

Increase in metabolic efficiency on cold exposure is also illustrated by the work of Beaton (1963a,b). He observed the growth, body fat content and other features of young laboratory rats for a week at 22° and 2° . On a diet containing 40% protein, the cold-exposed rats maintained body weight and synthesized fat, whereas others, on 20%

or 5% protein, did not. This suggests that, contrary to other reports, a high protein diet is advantageous for a rapidly growing rat in a cold environment. The differential effects of the various diets were, however, less in rats kept at 2° : for instance, (i) the rats fed on 40% protein ate the most of the three groups while at 22° but, on transfer to 2° , the others increased their food intake to the level of the 40% group (which did not change); (ii) the 5% group had a lower blood glucose than the other two groups at 22° but not at 2° at which temperature it was raised in all three groups. Beaton and Sangster (1965) have recently given further evidence of increased efficiency of protein utilization in cold-adapted rats.

C. SELECTION OF DIET

The experiments in which foods are forced on animals still leave open the question of the best diet for a cold environment; but mammals themselves, given a choice, might be able to select an optimum diet for survival or growth. Laboratory rats, at least, can, at ordinary temperatures, adjust their intake to their needs for certain salts and vitamins, as well as calories (reviewed by Barnett, 1963).

Donhoffer and Vonotzky (1947) gave laboratory mice a choice of three mixtures containing predominantly carbohydrate (starch), protein (casein), and fat (lard) respectively. At room temperatures, all three diets were eaten regularly, but more of the protein mixture than of the others. After 2–3 weeks, the mice were transferred to 10 – 11° . The consequent increase in food eaten was drawn almost entirely from the carbohydrate mixture. Görner (1956) found a similar preference for carbohydrate, rather than fat, at a low temperature, not only in house mice, but also in the wood mouse, *Apodemus sylvaticus*.

Little is known of the physiology of the change in appetite in an altered temperature. Animals do not change their intake at once to match the ambient temperature. Durrer and Hannon's (1962) dogs displayed no day-to-day correlation of calorie consumption with temperature (Fig. 3b). The rats studied by Donhoffer and Vonotzky took some days, after transfer to the cold, to reach their raised level of intake. Nevertheless, very brief, intermittent exposures to cold can influence food intake. Weiss (1958) exposed rats to 0° for only 20 min./day; controls were at 21° . Food consumption of the cold-exposed rats, during the hour after exposure, was low for the first 1–3 days; but, by about the eleventh day, it was much above that of the controls. A similar sequence in mice transferred to a cold environment is illustrated in Fig. 5. The low initial food intake of Weiss's rats was accompanied by decreased activity.

D. PROBLEMS OF FOOD CONSUMPTION

We now list some of the main factors which influence food intake in cold-exposed mammals. The first is genotype. Not only different species, but varieties of the same species, have different dietary needs, as Fenton (1960) has shown for mice. Secondly, age may alter needs; in particular, the demands of a rapidly growing young mammal differ from those of an adult. The same applies to pregnant and

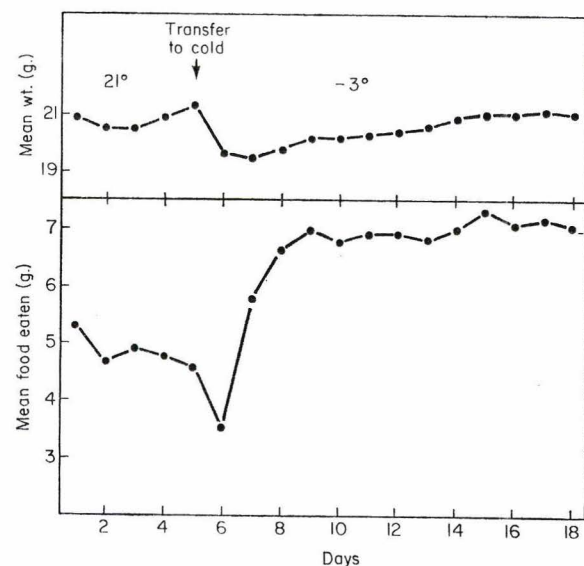


FIG. 5. Mean food consumption and body weights of ten mice, aged 5 weeks, transferred from 21° to -3°. There was a delay in the adjustment of food consumption to need.

lactating females. Little is known about the effects of any of these.

A further source of variation are the conditions experienced by the animal, from fertilization on. Uterine effects are discussed later (Section VI.C, p. 457). Adult laboratory rats or mice, transferred to a cold environment, go through a sequence of metabolic changes already described (Section II.C.2, p. 425). These changes may influence dietary needs. Moreover, mammals adapt their behaviour to circumstances: they may alter the amount eaten, the number of meals taken and their food preferences. Even for the much studied laboratory rat, nearly

everything remains to be learnt on all these features of adaptation to cold.

IV. Behaviour

A. "ACTIVITY"

Three features of behaviour concern us in this review: (i) feeding, which has been discussed in the previous section; (ii) "activity", which here means any movement of the whole body or of the trunk or limbs; and (iii) any behaviour which tends to reduce heat loss.

Decreased activity on exposure to cold is a general finding. The example of husky dogs (Durrer and Hannon, 1962) has been mentioned in Section III.A. p. 431. Ostermann (1956) observed a decline in activity during winter of four species of Muridae and three Gliridae. Zollhauser (1958) studied wild and laboratory mice (*Mus musculus* and *Apodemus sylvaticus*) in the laboratory, in cages each on a suspended platform. A temperature of 8°, instead of that of the animal house, reduced activity especially when there was no nest. Barnett and Scott (1964) compared the movements of mice at 21° with others at -3° and fully adapted to the cold; the latter were less active.

The decrement in activity due to cold is a function of the extent to which an animal is adapted to the cold. Hart (1953) showed this by recording wheel-running in deer mice, *Peromyscus leucopus*: by adapting some of his animals to 10° instead of 21°, he increased their rate of running at temperatures below 0°. This illustrates the fact that gross locomotor movements do not necessarily contribute to the extra heat needed at low temperatures. Hart and Héroux (1955) demonstrated this also for lemmings, *Dicrostonyx groenlandicus*, and rabbits, *Oryctolagus cuniculus*, and Hart and Jansky (1963) for laboratory rats.

The effect of exercise, too, is influenced by cold adaptation: rats kept at 4° for four weeks, and then exercised, display greater vaso-dilation in tail and colon than controls kept at 4° for only one day (Thompson and Stevenson, 1966).

The term "decline in activity", used with reference to the researches quoted above, has a precise significance in each case; but it is not always the same significance. The presence of a running wheel or treadmill stimulates more movement than would be displayed in its absence (Eayrs, 1951; Zollhauser, 1958); hence the same animal might display a different effect of cold in a treadmill from that in a tambour-mounted cage. "Activity", as defined in the first paragraph of this section, varies with general exploratory behaviour, specific "appetitive" movements (provoked, for example, by hunger), and stereotyped activities such as hoarding objects in the nest (reviewed by Barnett, 1963). Ross and Smith (1953) record a decline in hoarding in laboratory mice exposed

to cold. Barnett and Scott (1964) observed two kinds of stereotyped behaviour, in both inbred and hybrid laboratory mice, at 21° and -3°. In the warm, the mice gnawed food in excess of their need, and also gnawed wood, in an apparently futile way; at -3°, though fully adapted, they did no such useless gnawing. Even nest-building with unfamiliar material (paper strips) was less efficient in the cold, though with cotton-wool (which was familiar) it was more efficient (Barnett, 1956).

There are vast gaps in our knowledge of the relation of activity to cold adaptation. It is not known how total activity (as defined) is related, in any natural or seminatural situation, to temperature and the competing demands of (i) economizing in heat loss and (ii) getting food. It is not clear how different forms of activity interact. In a given situation, with declining temperature, the intensities of different sorts of behaviour evidently diminish at different rates. The earliest to disappear are those which make no immediate contribution to survival.

B. THERMOREGULATORY BEHAVIOUR

Although activity (as defined) does not necessarily contribute to thermoregulation by producing extra heat, specific movements may put the animal in a warmer, or better insulated, place.

Herter (1941) has reviewed a long series of experiments on the "thermotactic optimum" of various land animals. The mammals he used were laboratory mice. In a passage with a temperature gradient, the mice settled at a preferred floor temperature of 34-37°. Stinson and Fisher (1953) put deer mice, *Peromyscus maniculatus*, in an aluminium tube. When it was at a uniform temperature, they settled at the ends; in a gradient from 6° to 50° they did not respond very uniformly, but their preferred temperatures were between 20° and 30°; individuals, however, were fairly consistent when tested several times. This, like some aspects of feeding behaviour (Section III.A, p. 430), is an example of the way in which behaviour is sometimes unequivocally homeostatic in function: a mouse (or other mammal—the domestic cat is a familiar example) is restless if the temperature of its skin departs from a certain range. This is another instance of so-called "appetitive" behaviour; it can lead the animal to a warmer place (or a cooler one) in which it settles; hence the animal achieves a "consummatory state".

No doubt there are species differences in the thermotactic optimum. Herter (1941) even reports genetically determined differences between strains of laboratory mice. But we know little about the extent or causes of variation in preferred temperature. Temperature certainly influences behaviour early in life. Mount (1963d) finds that infant pigs,

Sus scrofa, prefer a temperature of about 30°. Nestling rats are provoked to squeaking by lowered temperature, as when they stray or fall from the nest (Wiesner and Sheard, 1933). An obvious gap in our knowledge is the effects of exposure to a cold environment on preferred temperature. Since we do not know how "thermotactic" behaviour develops, it would be rash to assume that it is highly stable in development and constant within each species.

There is some information on the ways in which adaptive behaviour can contribute to the achievement of an optimum temperature. Clearly, once an animal has discovered a warm or insulated place, it will tend to return to it, but laboratory rats can learn to do more than this. Weiss and Laties (1960, 1961) have observed rats in a modified Skinner box, in which pressing a lever switches on a source of heat for a fixed period. At a low temperature, the animals spent most of the first 5 hours or so crouching in a corner and shivering; they occasionally pressed the lever, but only casually. Then there was a sudden change in behaviour, and the heat was switched on regularly, at intervals determined by the amount of heat given and the surrounding temperature. This sort of behaviour is also adjusted to internal state: rats short of pantothenic acid, and hence with a low tolerance for cold, press the bar correspondingly more often (Weiss, 1957). In a similar situation pigs, *Sus scrofa*, too, will press a lever to turn on a source of heat, but a steady response rate is established more quickly (B. A. Baldwin and D. L. Ingram, personal communication). Here we have trial-and-error behaviour contributing to homeostasis.

A special case of apparently thermotactic behaviour is huddling. Probably all small mammals, and many large ones, sleep and rest in contact with others, when they can. Huddling is crucial for the survival of the young of small mammals when the temperature outside the nest is low (Section VIII, p. 465). It can also contribute to thermoregulation, or at least reduce the amount of food needed, in adults. Prychodko (1958) recorded food consumption in laboratory mice at -3°, 4° and 25°; some mice were alone, some in pairs and some in groups of five. In the warm there was only a slight effect of grouping; but at the low temperatures the sparing effect on food consumption was very marked: at -3° the presence even of a single companion decreased food consumption by about 18% (Fig. 6). Pearson (1960) estimated calorie and oxygen consumption in a harvest mouse, *Reithrodontomys megalotis*: oxygen consumption was at a minimum of 2.5 ml./g.hr. at an ambient temperature of 33°; below thermal neutrality, each decline of 1° led to an increase in oxygen consumption of 0.27 ml./g.hr.; but if three mice were put together at 1°, there was a decrease in oxygen consumption of 28%. Mount (1960) found a reduction, due to huddling, of about

30% in the oxygen consumption of piglets. Sealander (1952) observed the contribution of huddling to the survival at low temperatures of the deer mice, *Peromyscus leucopus* and *P. maniculatus*. At -23° the presence of a single companion greatly prolonged survival.

Many mammals display not only thermotactic behaviour but also what Darwin called "architectural instincts": nest-making is especially important for small mammals. Kinder (1927) gave laboratory rats strips of paper: the weight of paper used for making a nest increased as the ambient temperature was lowered. Barnett (1956) recorded the nests (made of cotton wool) constructed by laboratory mice fully adapted to,

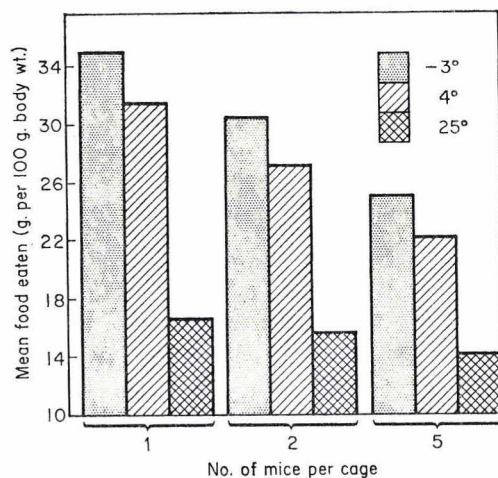


FIG. 6. Effect of ambient temperature and huddling on the daily food consumption of mice. (After Prychodko, 1958)

and breeding in, a room kept at -3° : as expected, they were superior to those of controls living at 21° . Important features of good nests were (i) the extent to which they were covered in; (ii) a domed shape; and (iii) fluffing of the cotton wool. Pearson (1960), in his work on harvest mice, found that a nest allowed a decline in heat production of about 20%. Thorne (1958) analysed one feature of nest-making in *Peromyscus maniculatus*, namely, the shredding of material (paper); these rodents shredded much more paper at 8° than at 21° . Hayward (1965) has illustrated the extent to which the burrowing habit of this species protects it from the fluctuations of the outside temperature (Fig. 7).

Nest building is influenced not only by outside conditions but also by internal state. A pregnant or parturient female, of a nest-making species,

always builds a good nest, but this affects the thermoregulation of the young rather than the mother. Interference with the endocrine system can, however, increase the nest-building even of males, by reducing ability to adapt to cold by other means. Richter (1937) reviews early work on the effects of thyroidectomy or hypophysectomy, both of which impair cold resistance and also induce laboratory rats to make better nests. Stone and Mason (1955) confirmed these observations on hypophysectomized male laboratory rats: assessed on an elaborate scale, these rats, at 15° , made much better nests than controls.

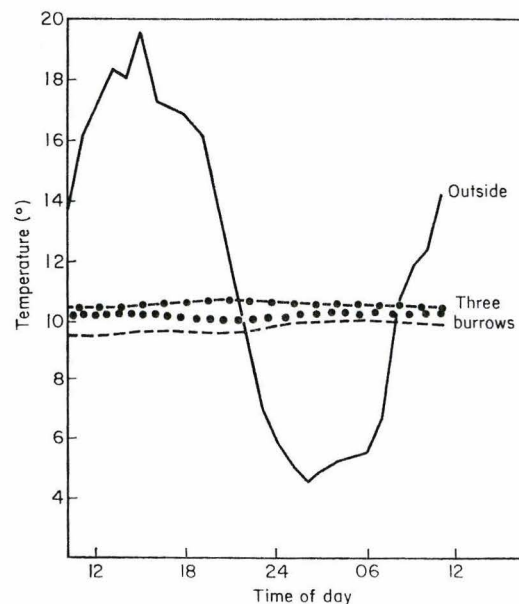


FIG. 7. Temperatures in three burrows of *Peromyscus maniculatus*, compared with those recorded outside in a 24-hr. period. (After Hayward, 1965)

Apart from maternal nest building, these observations all suggest a rather simple relation between huddling or nest-making on the one hand, and the thermal demands of the environment on the other. But in fact these two kinds of behaviour may be performed in the absence of the need to conserve heat: they are stereotyped activities, characteristic of many species and, like many other such activities, have a certain autonomy. The huddling of laboratory rats makes, in ordinary conditions, no contribution to conserving energy (Benedict, 1938).

Nevertheless, the immediate stimulation which induces huddling is probably the contact with a warm surface; huddling may, in fact, be an example of thermotactic behaviour even when it is not heat-conserving. The surface temperature of a mouse is near that chosen by mice in a gradient, for in air at 21° the temperature on the surface of the hair of a mouse is about 34°, while in air at -3° it is about 31° (Barnett, 1956). Features of a companion other than surface temperature could help to provoke contact but, if so, they are probably common to many species. Members of different species huddle together: an example is the association of *Rattus rattus* and *R. norvegicus* (Barnett, 1963).

The partial independence of heat conservation, displayed by nest-building, is even clearer. There are two aspects to this, one special and one general. The special aspect appears in the work of Gelineo and Gelineo (1952) on the ambient temperature preferred by lactating laboratory rats: this is 16°, far below thermal neutrality; if the ambient temperature rises to about 20°, the female moves the nest.

The general aspect is the autonomy (already referred to) of species-characteristic behaviour such as nest making, that is, the performance of the behaviour even when it has no homeostatic effect. Barnett and Scott (1964) gave mice 24 paper strips which could be drawn into the cage. This was done, on the average, more readily when there was already a well constructed cotton wool nest in the cage: the existing nest was then lined with paper, sometimes after shredding. Low temperature, in the conditions of these experiments, did not increase the rate of nest-building with paper; often it diminished it. This was perhaps due to the unfamiliarity of the paper strips, for the mice had had no experience of using them to conserve heat.

Although, therefore, the behaviour described in this chapter is all homeostatic in function, it does not follow that it is directly and simply related to need on every occasion. In the example just given, a learning process was evidently needed, before the standard patterns of drawing material to a nest site, shredding it and arranging it, could be performed in a way which corresponded to need. The obverse of this is the fact that nest-making and huddling may both occur in the absence of the need to conserve temperature.

V. Growth and Body Composition

A. NATURE OF "TROPIC" RESPONSES

Exposure to cold below the critical temperature usually entails an alteration of body weight or of the rate of total growth. These effects are always accompanied by less evident changes in the relative weights of

organs and in body composition. Three types of process are involved. First, material may be diverted from anabolism to heat production. This applies both to food and also to reserves already in the tissues. Second, certain organs may enlarge, evidently as a result of the extra work thrown upon them by the increased metabolic rate. Such enlargement may be expected in, for example, liver and gut, and some endocrine organs. Third, some structures are provoked to extra growth by cold, though not, presumably, as a result of having to do more work. This applies to some of the components of skin (Section II.C.4, p. 428). All these adjustments are reflected by changes in body composition, of which those in fat content are among the most obvious.

The changes in individual mammals after exposure to cold must be distinguished from differences between species or varieties which influence resistance to cold. If animals of one type have, for instance, a lower ratio of surface area to volume than those of another then, other things equal, the latter will be at a disadvantage in the cold. "Bergmann's rule" states that members of a taxon tend to be larger in the colder regions of its distribution (Bergmann, 1847); according to "Allen's rule", the colder the environment, the shorter the appendages and the more compact the body. Scholander (1955) has critically reviewed these beliefs. In this section, we discuss, not genetically determined differences in growth, but those imposed on individual mammals making their own physiological adjustment to a cold environment.

The scattered information on this topic has been reviewed by Hart (1957), Héroux (1961, 1963), Smith and Hoijer (1962), and Kleiber (1963). Héroux and Gridgeman (1958), and Angervall and Carlström (1963), have discussed some of the statistical hazards of the analysis of relative growth. Here we try to bring out the principles which underlie the facts.

B. BODY WEIGHT AND FOOD RESERVES

1. Changes in Total Weight

Assuming a constant shape, an adaptive change in total weight on exposure to cold must be an increase. Sealander (1951) found one species of *Peromyscus* to be heavier by about 2.5 g. in winter than in summer; but another species was unchanged in weight; and Hayward (1965), in an extensive study of *Peromyscus* from north-eastern North America, recorded lighter weights in winter (the winter mice may have been younger than the summer ones). *Rattus norvegicus* evidently keeps the same mean weight, summer and winter, in Canada (Héroux, 1963). For large animals, loss of weight is less serious than for small

15+7.

ones. Sheep lose weight in winter, especially if kept out of doors (Armstrong *et al.*, 1959). The still larger Brahman cow, however, at two years, exposed to winter temperatures down to -13° , merely reduces her growth rate (Ragsdale *et al.*, 1950).

Most of the information on the effects of cold on body weight is from work on small laboratory mammals. Below we distinguish five groups of relevant facts.

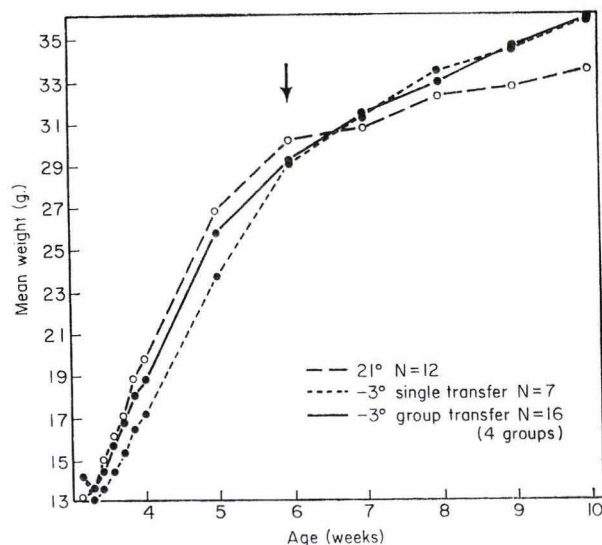


FIG. 8. Changes in the body weights of random-bred mice after exposure to cold. Controls were kept singly in an ambient temperature of 21° . Experimental mice were transferred at three weeks to -3° (with bedding) either singly (\cdots) or in groups of 4 (—). At six weeks, the experimental mice were returned to 21° . The curves show the immediate effect of the cold on growth, the effect of grouping, and a favourable effect of cold exposure on subsequent capacity for growth.

(i) Héroux (1961) has summarized the literature on the effects of transferring laboratory rats from around 20° to about 4° , cavies, *Cavia cobaya*, to a rather higher temperature, and hamsters, *Mesocricetus auratus*, to 6° . In these experiments, the animals are usually caged singly without a nest, and they have no opportunity to make a gradual adjustment to cold. The immediate effect is loss of weight, but survivors may begin to make up the loss after a few days. Figure 5, p. 436, illustrates this sequence from laboratory mice, and also shows the typical accompanying changes in food consumption.

(ii) Adults may never completely make up the initial loss of weight on cold exposure, but young, rapidly growing, mammals, if they survive the first few days, may be expected to resume growth, though at a lower rate (e.g. Barnett *et al.*, 1960). Figure 8 illustrates the responses of just-weaned laboratory mice to two kinds of cold exposure.

(iii) Barnett and Scott (1963) and S. A. Barnett (unpublished observations) have recorded the effects on body weight of breeding mice permanently in an environment at -3° . The mice made nests of cotton wool. When growth is recorded from birth, or from weaning, one may study the relationship between maternal performance and development of the young. The masses of litters at birth and weaning, in a polytocous mammal such as the mouse, may indeed be used as indices of maternal performance. Body weight, at least in early life, is influenced not only by the physical environment, uterine conditions, milk supply and maternal care but also by number in litter. Usually, body weight at weaning declines with an increase in size of litter. This effect of "competition" (presumably for milk) among litter mates (Biggers *et al.*, 1958) may be enhanced by cold (Barnett and Manly, 1959). Hence a full account of the effects of cold on body weight in the early life of a small mammal requires a statement of the regression of body weight on number in litter.

After weaning, the course of growth in a cold environment reflects that in the nest: mice already slightly stunted by very early exposure to cold continue to grow at a lower rate than controls (Barnett and Scott, 1963; but contrast Fig. 8).

(iv) This raises the question of the effects of cold in early life on later growth in a more favourable environment. Barnett and Scott (1963) transferred some of their mice from -3° to 21° , where they kept them in small groups. There was no compensatory growth. The mice, initially lighter than controls reared at 21° , remained so. However, much more information is needed on the effects of exposure at different ages, as Fig. 8 shows. After a period of undernourishment, a mammal may or may not make up the lost weight, according to (i) the severity of the deprivation, and (ii) the age at which it occurred (reviewed by Wilson and Osbourn, 1960). At certain ages, an unfavourable environment may set an animal's growth capacity for life (e.g. Widdowson and Kennedy, 1962). Exposure to cold in early life may have effects very similar to those of food shortage.

(v) There may be substantial genetical variation, within a species, in growth in a cold environment. Most laboratory mice, if reared at an ambient temperature of -3° , would probably be lighter than controls of the same strain reared at 21° . However, C57BL mice display no such difference (Barnett and Scott, 1963). More important, the same authors

crossed inbred mouse strains. The growth of the three types of F_1 mice produced in this way was not depressed by cold; and at -3° all three were heavier than parent strains, that is, they displayed "luxuriance" or "growth heterosis".

Genetical variation allows selection for resistance to cold, and this may have an effect on body weight (Fig. 9). A genetically mixed stock of laboratory mice was selected for ability to breed in the cold; after twelve generations these mice were heavier than controls kept at 21° (Barnett and Scott, 1963).

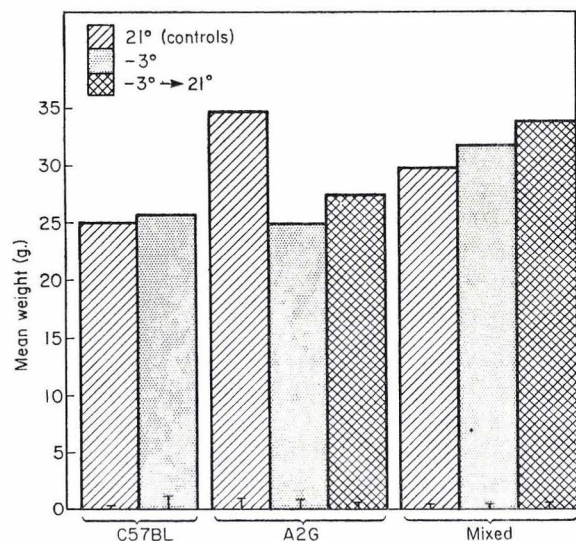


FIG. 9. Effect of environmental temperature on the body weights of male laboratory mice aged sixteen weeks. Mice at -3° were born and resident in that ambient temperature. Mice moved from cold to warm (21°) were reared at -3° for their first three weeks. Low environmental temperature had no effect on the body weight of the highly inbred C57BL mice, but a large effect on the A2G mice (also highly inbred); A2G mice transferred to 21° at three weeks did not recover from the effect of being reared at -3° (Contrast Fig. 8.). The genetically mixed stock at -3° had been selected for twelve generations for reproductive success at that temperature; this resulted in their being heavier than the controls bred at 21° . Vertical lines represent standard errors. (After Barnett and Scott, 1963)

2. Energy Reserves

Changes in gross body weight are accompanied by changes in the relative weights of tissues and organs; hence body weight is only a crude index of physiological function. The most labile structure is adipose

tissue. It is not only metabolically active, but is also capable of changing enzymically in response to demand (reviewed by Shapiro, 1963; Masoro, 1963, 1966). Accordingly, in this section we are concerned, not with its insulative role in cold-adapted species, but with its function as a reserve of energy. It is, however, not the only tissue reserve of energy: during cold adaptation, reduction in the mass of the muscles may lead to a substantial loss of body weight, at least in laboratory rats (Héroux and Gridgeman, 1958).

The body fat of some species alters seasonally. *Peromyscus leucopus* may have more than three times as much fat, relative to body weight, in winter as in summer (Sealand, 1951). Wild *Rattus norvegicus* in Canada may increase their abdominal and subcutaneous adipose tissue by 30% in winter (Héroux, 1963). These accumulations perhaps have some insulative or heat-storing function, but they are probably most important as food reserves. Certainly, fat stores are rapidly depleted on sudden exposure to severe cold, as well as in starvation: this depletion can be responsible for a large part of the loss of weight which follows exposure of laboratory mammals (reviewed by Héroux, 1961).

Pagé and Babineau (1953) exposed laboratory rats to a temperature between 3° and 10° ; energy expenditure was nearly doubled, and there was loss of fat which accounted for about 30% of the total weight loss. Male laboratory rats were studied by Héroux and Gridgeman (1958): after four weeks at 6° , they had about half the body fat of rats kept for four weeks at 30° ; this represented about one-fifth of the difference in total body weight. This was by far the largest percentage loss of any tissue or organ. Hart and Héroux (1956) exposed laboratory mice to -7° or -13° for four days; 85–89% of the reserve of energy used came from fat. Nevertheless this source provided only 15–20% of total energy needs during that period. Most of the heat produced still came from the combustion of the carbohydrate in the food.

The loss of fat on cold exposure does not necessarily persist. For instance, adult laboratory rats exposed to 11° lose fat during the first month, but later restore it (Babineau and Pagé, 1955). This sequence may be compared with that of the enzymic changes described in Section II.C.2, p. 425.

Continued exposure may, however, reduce the growth of adipose tissue after cold adaptation has taken place. Young and Cook (1955) put male Swiss mice at 4° for about seven weeks. These mice stopped growing, and ended with fat weighing about 4.8% of the whole body; the figure for controls at 24° was 10.5%. Barnett *et al.* (1959) and Barnett and Widdowson (1965) studied A2G mice breeding at -3° ; these mice were kept in groups and had nests. Females of the first or second generations in the cold weighed less than controls at 21° ; the decrement

corresponded to the difference in body fat content (Table I) but, as we shall see later, there were other differences in the constitution of the body. In males, although the difference in body weight of the A2G mice was even greater, the difference in fat content was less. This may be related to the fact that control females had about twice as much fat as control males. This strain is probably typical of laboratory mice. The C57BL strain, already mentioned as differing in total growth, also has a quite different fat metabolism (Table I).

TABLE I. *Body Weight and Fat Content of Virgin Female Mice Aged 16 Weeks: Means with Standard Errors (Barnett and Widdowson, 1965 and Unpublished Observations)*

Strain	Temperature (°C)	No. of Mice	Body Wt. (g.)	Body Fat	
				(g.)	(g./100 g.)
A2G	21	16	24.4 ± 0.2	3.5 ± 0.2	14.1 ± 0.7
	-3	13	21.8 ± 0.3	1.8 ± 0.1	8.5 ± 0.3
C57BL	21	12	21.5 ± 0.4	1.8 ± 0.2	9.2 ± 0.8
	-3	9	21.6 ± 0.6	1.9 ± 0.2	8.7 ± 0.9

A disadvantage of estimations of total fat content is that they take no account of the different types of adipose tissue. An important distinction is between brown and white adipose tissue (reviewed by Johansson, 1959; Smith, 1964). These are not readily distinguished by the naked eye, but the former differs from white tissue in the following ways. (i) The yellowish colour, which turns to brown if much fat is lost, is due to a high content of respiratory pigments. (ii) It is present in the rat especially in the interscapular region of the back, in the neck, and dorsal to the kidneys. (iii) It is exceptionally labile: the fat, which within each cell forms many small vacuoles surrounded by mitochondria, is quickly converted to fatty acids; these are readily oxidized. The heat so produced is evidently an important means of thermoregulation in small mammals suddenly exposed to cold. (iv) During prolonged exposure to cold, brown fat undergoes hyperplasia, and heat production from this source rises correspondingly.

Brown adipose tissue is active in young mammals. Dawkins and Hull (1963) and Hull and Segall (1964, 1965) state that it is an important site of heat production in new-born rabbits. It may also contribute largely to thermogenesis in human infants (Aherne and Hull, 1964). Chaffee *et al.* (1964) find that the brown adipose tissue of cold-adapted hamsters, *Mesocricetus auratus*, has a greater heat-producing capacity than that of controls; this is accompanied by changes in enzyme activity.

Emphasis on brown fat should not lead to a neglect of white adipose tissue. This too constitutes a reserve of energy. Indeed, within the brown tissue there are cells with the structure typical of the white and, during cold exposure, these give up their fat as well; in a laboratory rat exposed to 6° for four days, they have almost disappeared from the interscapular tissue (Cameron and Smith, 1964). No doubt the larger masses of plain white adipose tissue give up their fat over a still longer period, if an energy deficit persists.

C. GROWTH OF APPENDAGES

Loss of fat, or of weight from any other cause, is disadvantageous in a cold environment, but other changes in bodily proportions seem to be adaptive.

The length of the tail and the ears, and the length of the body relative to body weight, may all be reduced by rearing laboratory rats or mice in a cold environment (Sumner, 1909, 1915; Przibram, 1923; Emery *et al.*, 1940; Chevillard *et al.*, 1962; Barnett, 1965b). Moreover, the mouse tail lengthens in a hot environment (e.g. Harrison, 1963). Harrison (1958) cut off the tails of mice and found that this lowered their tolerance to an ambient temperature of 32°. There is also now no doubt that the rat tail is an organ of thermoregulation: its blood vessels dilate in a warm environment, and this greatly increases heat loss from the surface; the same thing happens in the feet, but not the ears (Rand *et al.*, 1965; Thompson and Stevenson, 1965).

Much remains to be discovered about the growth of the hairless Murid tail in different environments, and also the effects of selection on it. Barnett (1965b) found a shortening effect of cold, not only in mice with tails of typical length, but also in mice with genetically short tails. There was a decrease in size without a major change in proportions; but cold evoked a slight reduction in the number of tail vertebrae. However, he also studied mice of a genetically mixed stock selected in a cold environment for eighteen generations; these mice, already mentioned as being heavier than controls after twelve generations, developed *longer* tails than the controls at 21°. Probably the shorter tails in cold environments are an incidental result of the action of the low temperature during development, with little or no adaptive significance.

D. ADAPTIVE GROWTH

1. *The Organs Affected*

The increased respiration, food consumption, intermediary metabolism and excretion, which result from exposure to cold below the critical temperature, must require certain organs to do much more work.

Endocrine organs, especially thyroid and adrenals, constitute a special case of adaptive growth in cold-exposed mammals, and they are referred to separately (Section II.C.3, p. 427). Of the larger organs, there is no good evidence that the lungs are affected (Hérroux and Gridgeman, 1958), but the heart, gut, liver and kidneys all tend to enlarge. The evidence for this, mostly from laboratory rats, has been summarized by Hérroux (1961). Since then Chaffee *et al.* (1963) have observed a 30% rise in absolute kidney weight in hamsters, *Mesocricetus auratus*, exposed (without nests) for about nine weeks to 5°. Barnett and Widdowson (1965) have reported on the weights of organs of mice of the first or second generations breeding (with nest material) at -3°: regressed weights of stomach, small intestine, liver and kidneys were, as expected, greater than those of controls at 21°; there were, however, some differences in detail between the sexes.

In the usual type of laboratory experiment, the animals are inbred or at least domesticated; and they are suddenly exposed to cold alone and without protection. In nature, the onset of cold is usually gradual; and a wild population is genetically very different from a domestic one. These differences certainly influence the effects of cold on rats (Table II). The significance of the failure of wild rats to have enlarged livers or kidneys in winter is uncertain: perhaps these organs are more efficient per unit weight than those of laboratory rats, at least in winter; in more severe cold they might enlarge, as do those of the laboratory strains.

One other large organ undergoes changes on exposure to cold, namely, the pelt. In large arctic mammals, such as the wolf, *Canis lupus*, and the black bear, *Euarctos americanus*, insulation improves in winter (Hart, 1956). Durrer and Hannon (1962) find that husky dogs have a thicker hair coat in winter. In small mammals there is little scope for improvement in insulation from skin or hair, since a great increase in either would immobilize a mammal the size of a mouse. Nevertheless, mammals evidently have a general capacity to grow thicker hair in cold conditions; but this does not apply to the skin, since this is liable to become lighter on exposure to cold: indeed, total insulation from skin and hair may decrease in a cold environment in the laboratory (Hart, 1957; Barnett, 1959). Here again Hérroux has demonstrated a difference between the effects of laboratory experiments and those of seasonal cold (Table II).

A general effect of prolonged exposure to cold is a proportionate increase in actively metabolizing tissues, such as liver and gut. Hence cold-adapted laboratory mammals usually contain more water than controls: this holds for rats (Deb and Hart, 1956; Baker and Sellers, 1957), hamsters (Farrand, 1959) and mice (Barnett and Widdowson, 1965). There is a corresponding decline in the proportion of nitrogen

TABLE II. *Changes in Rats Exposed to Cold (after Hérroux, 1963)*

	Laboratory Rats		Wild Rats
	indoors	outside	natural habitat
Total growth	-	-	+
Adipose tissue	-	○	+
Liver weight	+	+	○
Kidney weight	+	+	○
Heart weight	+	○	+
Pelt insulation	○	+	+
Resting metabolic rate at 30°	+	○	+

The laboratory rats were exposed, in groups, either (a) to continuous cold indoors or (b) to seasonal cold outside. The wild rats were trapped. ○, indicates no difference; -, a decline in cold; +, an increase in cold.

(that is, in effect, protein) in the body. The connective tissues also bulk rather less; this is reflected in a lowered collagen content. The relative weight of the skeleton, too, indicated by the calcium content of the body, tends to be lower; but in this there is a difference between the sexes, since virgin females are less affected than males (Barnett and Widdowson, 1965).

There are also shifts in electrolyte balance (Baker, 1960a,b). During the early stages of cold adaptation, rats retain some sodium and, to a smaller extent, potassium. There is a very brief initial period of chloride loss. In man, the blood also becomes more concentrated. After some weeks the picture is different, just as it is in other respects: blood volume is raised above the control level, and plasma potassium and chloride have returned to the normal range; but plasma sodium remains high. The significance of these changes is not yet clear: they need to be linked with the other processes of cold adaptation.

2. Problems of Function

Differences in the gross weights of organs, or in total body composition, can only hint at the means by which a mammal becomes adapted to cold. Their limitations include the following: (i) an organ can become more efficient without an alteration in weight; (ii) total weight does not indicate which tissues are changed by cold.

The fact that an organ, such as the kidney or thyroid gland, can become more efficient per unit weight has been discussed by Abercrombie (1957) and by Goss (1964). The evidence comes from experiments in which compensatory growth occurs after removal of tissue; if a large part of a kidney is removed, regeneration follows, but the original weight is not fully restored though function is. Something of the sort may occur

during adaptation to cold. Barnett and Widdowson (1965) give the weights of the kidneys of three classes of A2G mice: (a) controls at 21°, (b) mice of the first or second generations reared at -3°, (c) mice of the fourteenth generation at -3° (Table III). Absolute weights were lower in both experimental groups, and even the relative weight was lower in the mice of long ancestry in the cold. Yet the latter were the better adapted to the cold environment (reviewed by Barnett, 1965a).

In a complex organ, hypertrophy or hyperplasia may occur in only some of the component tissues. In the kidneys of hamsters exposed to 5°, large numbers of mitoses appear after two days; this hyperplasia, which persists for some weeks, occurs principally in the proximal tubules: there is no general enlargement of the organ, and no new

TABLE III. *Weights of Bodies and Kidneys of Male A2G Mice aged 16 Weeks: Means with Standard Errors*

Temperature (°)	No. of Mice	Body Wt. (g.)	Kidney Wt.	
			(g.)	(g./100 g. body wt.)
21	14	28.7 ± 0.72	0.573 ± 0.014	2.00 ± 0.04
-3	17	24.0 ± 0.77	0.498 ± 0.037	2.07 ± 0.05
(generations 1 or 2)				
-3	12	27.5 ± 0.57	0.478 ± 0.015	1.73 ± 0.04
(generation 14)				

nephrons are formed (Chaffee *et al.*, 1963). Another example of (evidently) histological complexity is provided by the small intestines of the three classes of mice mentioned in the previous paragraph. The intestines of one group of mice in the cold were heavier than those of the controls, but not much longer; hence the amount of tissue per unit length was increased. But the mice of long ancestry in the cold had much the longest intestines. These differences require more detailed study.

Another kind of special hyperplasia occurs in the capillary systems of some organs (Héroux and St. Pierre, 1957). After four weeks at 6°, rats have about twelve times as many capillaries in their skeletal muscles as have controls kept at 30°. The capillaries of the ears undergo a similar increase, but—surprisingly—not those of the heart or liver.

3. Problems of Morphogenesis

The enlargement of organs, which constitutes a part of cold adaptation, raises difficult problems of the regulation of growth. The control of

compensatory regeneration and hypertrophy has been principally studied in animals from which large masses of tissue have been removed; and the control of skin growth has been investigated after wounding (e.g. Sandblom, 1949). These operations produce changes on a massive scale. Those of cold adaptation are by comparison small, but they may be of the same sort. This notion is supported by the observations of Chaffee *et al.* (1963), mentioned above, on the hamster kidney during cold adaptation. The distribution of mitotic figures, and the time of their onset, resemble those described by Williams (1961) during compensatory hyperplasia in the kidney of the rat. The “trophic” changes which take place during exposure to cold perhaps deserve investigation from this point of view.

VI. Reproduction

A. BREEDING SEASONS

Most mammals breed seasonally: young are born in spring or summer, and reproduction ceases in colder weather. In mammals, as in birds, the onset of breeding is probably unaffected by the temperature of the environment: day length is often crucial (reviewed by Fraps, 1962). Cold may induce a prolonged anoestrus, for instance in the golden hamster, *Mesocricetus auratus* (Grindeland and Folk, 1962); exposing laboratory rats to outdoor winter temperatures lengthens the oestrous cycle (Lee, 1926); and in the laboratory mouse, dioestrus is lengthened by environmental temperatures around 0° (Parkes and Brambell, 1928) or -3° (Barnett and Coleman, 1959).

In nature, small mammals which have no fixed breeding season perhaps stop breeding in autumn or winter as a result of a decline in the food supply. Little is known about such seasonal influences. Barnett and Coleman (1959) and Perrault and Dugal (1965) have suggested that the effects of cold and of food shortage are often similar. Perrault and Dugal, in a study of testicular function in cold and shortage of food, distinguish a systemic action from a specific endocrine effect. But there is little information on the effects of cold on the reproductive powers of males. A prolonged study has, however, been made of the reproductive performance of laboratory mice at -3° (reviewed by Barnett, 1965a), and this at least makes clear that males of several inbred strains can be fertile at that temperature. Most of this work, however, concerns females, and the rest of this section is confined to them.

B. REPRODUCTIVE PROCESSES IN FEMALES

The general effect of a cold environment on female reproductive processes is to slow them down (Figs. 10 and 11). The vaginae of

random-bred mice, born in a room kept at 5°, open later than those of controls at 21° (Biggers *et al.*, 1958). Inbred A2G mice of a stock breeding at -3° had a mean age of vaginal opening of 33 days, while the control figure was 26 days; in both groups, mean body weight at opening was 13 g. (Barnett and Coleman, 1959). There is evidently a correlation between vaginal opening and the processes which regulate total growth.

The effects of cold on the oestrous cycle are less simple. A2G mice have a mean age of onset of typical oestrus of 38 days at 21°, but of 61 days at

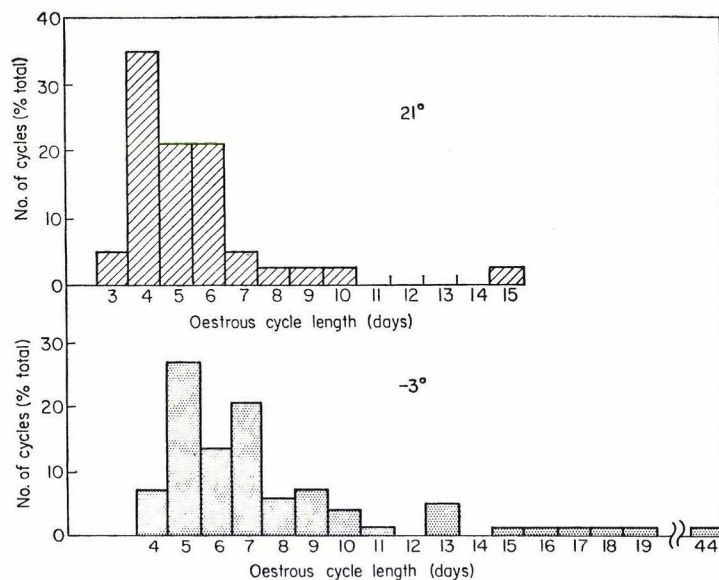


FIG. 10. Lengthening of the oestrous cycle of virgin female A2G mice by a cold environment. The mice at -3° were born in that ambient temperature. Based on 79 cycles at 21°, and 82 cycles at -3°. (After Barnett and Coleman, 1959)

-3°. Thereafter, females kept in groups have mean cycle lengths of 4.8 and 8.5 days, respectively (Barnett and Coleman, 1960). Emery *et al.* (1940) recorded longer oestrous cycles, and briefer oestrus, in laboratory rats exposed to 1.6° for 16 hr. each day. These facts fit into the picture of slower reproductive processes in the cold (Fig. 10), but those concerning mice transferred to the cold as adults do not. Transfer does lead to lengthened oestrous cycles, but only at first; after many weeks, the control length of 4.8 days is restored. Parkes and Brambell (1928) reported a similar finding in mice transferred to an environment at

about 0°. These observations suggest that cycle length in a cold environment with plenty of food reflects, not the temperature to which the adult is subjected, but that in which it was reared. Perhaps there is an early sensitive period during which cycle length is determined for life.

Corresponding to the late onset of oestrus, the first parturition is delayed in a cold environment; in two inbred strains the mean age for controls is about eleven weeks, while at -3° it is about seventeen

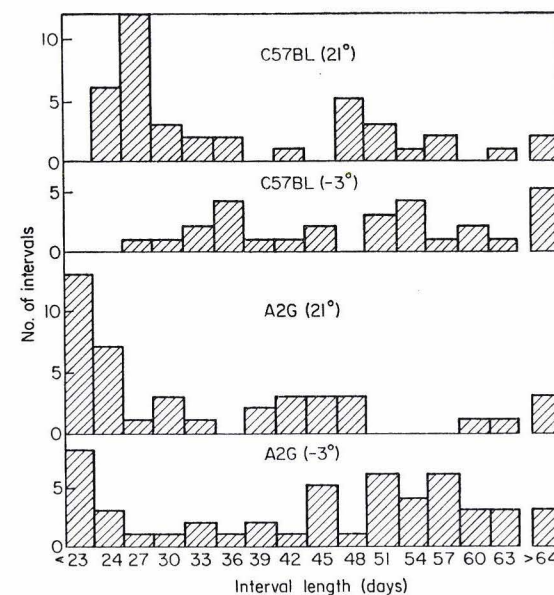


FIG. 11. Effect of low ambient temperature on the interval between parturitions of mice of two inbred strains. The mice in the cold were members of stocks bred in a room at -3°, and were in permanent male-female pairs.

weeks (Barnett and Coleman, 1960). Furthermore, when each female is kept permanently with one male, the interval between parturitions is longer in the cold; in strain A2G at 21°, about 60% of conceptions (apart from first ones) take place at post-partum oestrus, but at -3° about two-thirds occur around three weeks later, at post-lactation oestrus (Fig. 11).

Inevitably, the rate at which young are produced in a cold environment is lower than that in a warm one. From the facts just given, this would hold even if the number of young born and weaned per litter were

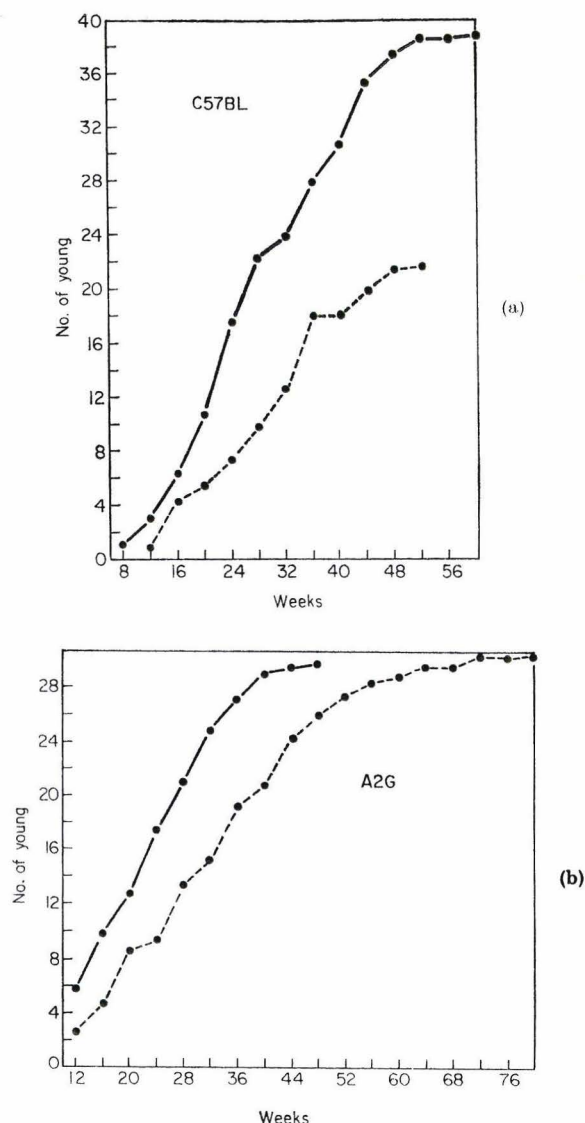


FIG. 12. Effect of low temperature on the number of young mice born per mated pair. Continuous lines indicate controls at 21°; broken lines, mice at -3°. (a) C57BL mice are shown to stop breeding at about the same age at both temperatures, and to be less fertile at -3°. (b) A2G mice, after many generations in the cold, continue to breed for about twice as long as controls, and so produce eventually as many young. (From Barnett, 1962)

unaffected by cold. It does not, however, follow that the total number of young produced per pair must be reduced. This is illustrated by a study of mice of strains C57BL and A2G which were allowed to breed until their reproductive capacity was exhausted (Fig. 12). The C57BL mice stopped breeding, in both temperatures, at about fifty weeks; hence their fertility at -3° was much lower than in the warm environment. The A2G mice at 21° stopped at about forty weeks; but, at -3°, they continued to about eighty weeks. Hence their total output of young was the same at the two temperatures. These A2G mice were of the eighth or ninth generations in the cold environment; had they been of the first or second generations, the outcome would have been different, as we shall see below. Unfortunately, there is not yet any information on the total performance of random bred mice in a cold environment.

C. THE MATERNAL ENVIRONMENT

The first environment of a mammal is a uterus, and the second—which is often a nest or lair—is one in which the mother remains the only source of food. The environment provided by a female for her foetal and nestling young is in turn affected by (i) the environment in which she lives; (ii) the environments in which she was reared; and hence (iii) the environments in which her mother lived. There is only the barest beginning of information on these relationships: for instance, the optimum ambient temperature for reproduction is not known even for laboratory mice. C57BL mice, given nest material, wean more young per pair at 10° than at 21°, though other strains do better at 21° (Barnett and Manly, 1956, 1959; Barnett, 1964).

From the works just quoted, a summary may be made of the effects on fertility of transferring mice from 21° to -3° at puberty. The number of young born per litter is reduced, often by about one-third. This probably reflects conditions *in utero*, rather than ovulation rate; but on this more needs to be found out. Much the same applies to breeding among the *offspring* of mice transferred in this way, that is, of the first generation born and reared in the cold. There is, however, one important qualification: maternal performance in this generation is inferior to that of the females of the transferred generation; this is evident from the weights of the young at three weeks (Table IV). Correspondingly, mice reared at -3° and transferred to 21° at mating have lighter young than controls at 21° (Barnett and Manly, 1959). Other evidence of such maternal effects is summarized by Barnett (1965a). Clearly, in the conditions of the experiments on these mice, it is a disadvantage for a female mouse to be reared in a cold environment. Chevillard and Cadot (1963) have observed an analogous decline in

fertility in laboratory rats bred for three generations at 5°. Their animals, however, gave no evidence of recovery: there was therefore no possibility of continued breeding in the conditions they used.

TABLE IV. *Maternal Effect in A2G Mice: Advantage Resulting from Parents Having Been Reared in a Warm Environment. Means with Standard Errors. (From Barnett, 1961)*

	(a) Transferred from warm to cold at mating	(b) Offspring of (a)
Fecund pairs	8	5
Born per pair	16.6 ± 2.8	12.2 ± 2.5
Born per litter	5.5 ± 0.5	5.5 ± 0.6
Weaned per weaned litter	5.4 ± 0.3	5.0 ± 0.7
Weights of young at 3 weeks (g.) $\left\{ \begin{array}{l} \delta \\ \text{♀} \end{array} \right.$	9.3 ± 0.2 8.7 ± 0.1	7.7 ± 0.2 7.6 ± 0.3
Barren pairs	1	4

D. GENETICAL VARIATION

The laboratory animals most used in physiological experiments are often highly inbred. Members of such strains may be referred to as "the mouse", "the rat" and so on, but this is misleading. First, inbred strains differ among themselves; second, laboratory animals always differ genetically from the wild forms of their species; third, inbred populations offer little scope for genetical change due to selection; and fourth, homozygosity, due to inbreeding, generally reduces fertility and other components of fitness. These matters have been more fully discussed elsewhere (Barnett, 1965a).

Some minor effects of selection for fertility at -3° have been observed in a mixed stock of laboratory mice (Barnett, 1961; Barnett and Scott, 1963). Body weight increased, but adipose tissue declined. The number of young born and weaned per pair rose substantially over twelve generations. Mortality in the nest declined from over 40% to below 10%. We shall see in the next section that not all these changes were necessarily due to selection of favourable genotypes; but some of them probably were.

A slightly less obvious genetical principle is illustrated by the performance in the cold of F₁ mice, produced by mating two inbred strains. Such mice display "hybrid vigour" in an ordinary environment; and this superiority over inbred animals may be enhanced in unfavourable conditions. For example, mice of the cross C57BL × A2G at 21° rear twice the weight of young produced by their parent strains; but at -3°

they rear nearly five times the weight produced by the parent strains (Barnett and Coleman, 1960). Hence heterozygosity may be especially important in an adverse environment. This is also exemplified by the resistance to cold of young mice: among all possible crosses between four inbred strains, nearly all the F₁ types were superior to the inbred parent strains (Barnett, 1964).

E. CUMULATIVE EFFECT OF COLD

It would be expected that, after one or two generations, inbred animals in a cold environment, unlike the mixed stock of mice referred to above, would show no progressive change in reproduction or growth. But in fact, a progressive decline in nestling mortality, over several

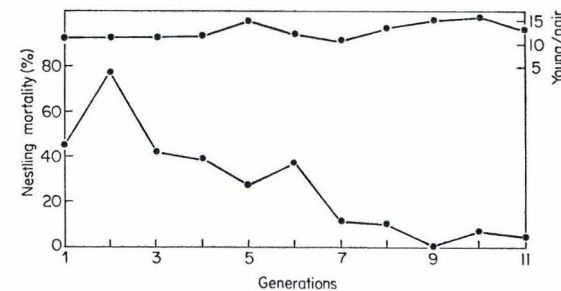


FIG. 13. Decline in nestling mortality among A2G mice bred for eleven generations in an ambient temperature of -3°. The total number of pairs was 57. The number of young born per pair remained steady. Controls bred at 21° did not display any such improvement. (After Barnett, 1961)

generations, has been observed among mice of inbred strains A2G and C57BL at -3° (Barnett, 1961). These mice differed from the mixed stock (referred to above) in retaining a steady rate of number of young born over the generations (Fig. 13). There was no corresponding improvement among the controls at 21°. Mice transferred to a cold room on later occasions again had a high nestling mortality; hence the decline in mortality was a property of the permanently cold-bred stock, and not a temporary consequence of the conditions in which they were kept, or of any factor acting at both temperatures.

The A2G mice bred for many generations in the cold differ from recently introduced mice also in growth properties (Table V) and in several aspects of maternal efficiency (Barnett and Little, 1965; Barnett and Widdowson, 1965). A progressive, adaptive change in an adverse environment, such as this, suggests selection of favourable genotypes, but there is little scope for this in inbred strains. There are in fact

TABLE V. *Effects on Male Mice (Strain A2G) of Long Ancestry in a Cold Environment (After Barnett and Widdowson, 1965).*

[○ Indicates no Difference from Controls; +, an Increase; - a Decrease]

	Generations 1 or 2	Generation 14
Body weight	-	○
Body fat	○	+
Body water	+	-
Nitrogen	-	○
Collagen	-	○
Calcium	-	○
Heart	+	+
Stomach and intestine	+	○
Liver	+	○
Kidneys	○	-
Testes	+	○

overwhelming reasons for rejecting a genetical explanation of the change (Barnett, 1960, 1961). Improbable though it seems, a cumulative maternal effect must be sought, to account for the secular changes in at least the two inbred strains.

The principal fact is that inbred mice have become better adapted to a cold environment as a result of breeding there for a number of generations. This unexpected observation, whatever the detailed explanation, shows that the cold adaptation of mammals may have features which cannot be fully revealed by short-term experiments.

VII. Ontogeny

A. HOMEOTHERMY AND HETEROOTHERMY

The homeothermic powers of new-born mammals vary greatly (reviewed by Gelineo, 1959). One of the smallest, the mouse, at birth completely fails to respond to cooling by a rise in metabolic rate (Fitzgerald, 1953). However, the new-born mouse displays a corresponding tolerance of hypothermia which is characteristic of mammals immediately after birth (McCance, 1959). The same applies to new-born rats (Campbell and Riccio, 1966). At the other end of the scale, the reindeer calf, *Rangifer tarandus*, is born while the herd is moving towards the sea in the spring; and it is so resistant to cold and so mature that, within minutes, it is accompanying its mother and keeping up with the rest of the herd.

Hart *et al.* (1961) have investigated the metabolic rates and body

temperatures of the closely similar infant caribou, also *R. tarandus*, in diverse conditions of temperature, wind and wetting of the fur. Thermoregulation is well established at birth. The metabolic rate is doubled by exposure to 0°, but a low temperature together with wind and wetting raise the metabolic rate to over five times the resting value. If, however, the calves have no protection, they can be made hypothermic, and so can die, if they are exposed to the extreme conditions prevailing during storms in northerly latitudes.

Most other animals lie between mice and caribou in this respect. The rat has been much investigated, notably by workers in Prague (see Hahn *et al.*, 1961). The rat was once thought to be heterothermous at birth (Fairfield, 1948), since it evidently does not increase its oxygen consumption on exposure to cold until it is 3-4 days old. But even new-born rats increase their oxygen consumption if they are moved from an environment at 36° to one at 29° or 30° (Gelineo and Gelineo, 1951). If they are kept at 30° for longer than about 30 min., oxygen consumption begins to fall. Taylor (1960) confirmed these findings, and commented that the large and abrupt drop from 35° to 20° in Fairfield's experiments led to cooling of the tissues and so prevented an increase in oxygen consumption. Taylor found that, during the first six days after birth, the critical temperature is between 33° and 38°. There is always a rise in oxygen consumption when the environmental temperature is lowered from 35° to 29°. The rise is small in unfed rats: the greatest metabolic response occurs soon after the rats have begun to feed. Barić (1953) had already found that, when rats of 4-5 days of age are fed, they behave like homeotherms in the ambient temperature range 30-37°; but when fasted they behave like heterotherms at the same temperature. Nevertheless their oxygen consumption at 37° is 1,800 ml./kg.hr. whether they are fed or fasted. At 30°, the rate increases to 3,100 when the rats are fed, but falls to 1,250 ml./kg.hr. when they are fasted.

Gelineo (1959) points out that the puppy, too, loses its capacity for homeothermy when starved, whereas starvation of a fully grown dog, even to the point of death, does not change the type of thermoregulation. More surprising, the new-born guinea-pig, *Cavia*, remains a homeotherm when starved. These rodents are born in a much more mature state than most others. Gelineo (1957) finds that thermoregulatory ability at birth increases in the order: rat, rabbit, dog, guinea-pig; the corresponding cold limits are 29°, 23°, 19° and 7° ambient temperature.

In some species, noradrenalin greatly increases heat production in the newborn. Moore and Underwood (1963) found this to be so in kittens, rats and rabbits; the effect declines with advancing age. Non-shivering thermogenesis in the new-born (Brück and Wünnenberg, 1965a) may be

related to the presence of brown fat (Dawkins and Hull, 1964; Dawkins and Scopes, 1965; Brück and Wünnenberg, 1965b; Hull, 1966; and see Sections II.C.1 and V.B.2, pp. 425 and 446).

B. METABOLIC RATE

Metabolic rate increases after birth, in thermally neutral and in cold conditions. This is true for the rat (Gelineo and Gelineo, 1951; Taylor, 1960), dog (Gelineo, 1957), ox (Roy *et al.*, 1957), pig (Mount, 1959), sheep (Dawes and Mott, 1959; Alexander, 1961), rhesus monkey (Dawes *et al.*, 1960), and perhaps in man. In our own species, however, the increase has been unequivocally shown only in cool conditions. Some workers have recorded a rise at thermal neutrality (Hill and Rahimtulla, 1965) but others have not (Brück, 1961; Karlberg, 1952). The increase in metabolic rate in the rat is rapid during the first 24 hours, and thereafter is more gradual up to three weeks. The most striking increase in response to cold occurs soon after a new-born rat begins to feed (Taylor, 1960). Correspondingly, Mourek (1962) found a large decrease in oxygen consumption in rather older rats at 26° after a 24-hour fast. The gradual rise in metabolic rate during the three weeks after birth is associated with improved thermoregulation.

In the new-born pig, there is a vigorous metabolic response, with shivering, when the environment is cooled; this increases as the temperature falls towards 0° (Mount, 1959). The cold limit for a solitary new-born pig, as opposed to a litter of huddled pigs, is about 5° when air movement is low (Mount, 1963a). The highest rate of heat production observed in any single pig is 162 kcal./m.²hr.; this was in an animal during the first week after birth. During the first few post-natal hours, however, the pig cannot approach this level. Oxygen consumption rises, over a wide range of ambient temperatures including thermal neutrality (above 34°), during the first 1–2 days after birth. This rise is accompanied by an increase in rectal temperature from a mean of 38.0° for the first post-natal day to 39.0° later.

The metabolic rate of new-born pigs, at the neutral temperature (34°), nearly doubles during the first two days after birth (Mount, 1961). In lambs, the corresponding increase is nearly threefold during the first day (Dawes and Mott, 1959). The oxygen consumption rate of rhesus monkeys at thermal neutrality nearly doubles during the first week; this is associated with a steady rise in rectal temperature during the first 3–4 days (Dawes *et al.*, 1960). These authors calculate that, in the lamb and the monkey, oxygen consumption per unit surface area in a thermally neutral environment rises during the early post-natal period, to a figure almost identical with that of an adult female. The same is true for the pig.

Brück (1961), Hill and Rahimtulla (1965) and Adamsons *et al.* (1965) found that the new-born full-term human baby responds to a cold environment by increasing its heat production. The figure for oxygen consumption rate at thermal neutrality just after birth found by Brück was similar to those obtained by Hill and Rahimtulla (4.8 ml./kg.min.) and by Adamsons *et al.* (4.6 ml./kg.min.). The basal metabolic rate of Hill's babies increased to 6.6 ml./kg.min. at 18–30 hours of age, and to 7.0 ml./kg.min. at 6–10 days, whereas Brück found no increase. Hill found the critical temperature to decrease from 36° at birth (a value close to that found by Adamsons *et al.*, 1965) to 32° at the end of the first week. In view of the results obtained with other species, the human infant's basal metabolic rate probably does rise in the days after birth. Both Hill and Brück found that metabolic rates in the cold increased with age.

A baby often remains at the same body weight for several days after birth; and it usually takes about six months to double its birth weight. The young of other species grow much more rapidly (Brody, 1945): even the new-born pig doubles its birth weight in about a week. Hence the metabolic rate of the baby clearly increases with age, since body weight changes only slowly; but the relation of metabolic rate to the post-natally rising body temperature is less certain (Hill and Rahimtulla, 1965). The situation is still more complicated in the new-born pig, since here body weight is changing as well. Mount and Rowell (1960) therefore applied multiple regression analysis to the oxygen consumption rates of pigs during the first five weeks after birth, in relation to body weight, rectal temperature and age. This allowed the relation of each of these variables to be assessed, while the other two were held constant. At ambient temperatures of 30° and 4° (that is, close to thermal neutrality and around the cold limit, respectively) heat production per unit body weight decreased with increasing body weight; but calculated per unit surface area it remained more uniform. Both body weight and rectal temperature had large effects on oxygen consumption in the first five weeks after birth. The effect of age was less marked: indeed, in pigs less than one week old there was no significant effect at all. In older pigs, oxygen consumption fell slightly but significantly with increasing age. This result does not mean that oxygen consumption decreases as the pig grows older; this is clearly not so, since the animal is increasing in size. It does suggest, however, that, among a number of pigs of the same body weight and rectal temperature, the older pigs will have a lower oxygen consumption. This may be related to better thermal insulation in the older animals.

The small effect of age indicates that thermogenesis in the pig is well developed at birth. In other species, time since birth has a marked effect

on the response to environment. In the rat, during the early post-natal period, age is an indication of the level of development of nervous control and consequently of the degree of metabolic response which the animal can make to changes in its environment (Adolph, 1957).

In the puppy, *Canis familiaris*, heat production increases during the first two weeks of postnatal life, but mechanisms of heat conservation lag behind (McIntyre and Ederstrom, 1958). This lag occurs in the pig as well. It may be related to the lack of subcutaneous fat at birth (Widdowson, 1950), coupled with the absence of an effective hair coat, since peripheral vasoconstriction in the cold does occur in the new-born pig (Mount, 1964a). Vasoconstriction in the absence of a fat layer has little effect (Section II.A, p. 414). A similar state of affairs exists in the human infant (Brück, 1961). The critical temperature falls in the first weeks of life in the pig (Mount, 1960), dog (Gelineo, 1954), rabbit (Hull, 1965) and baby (Hill and Rahimtulla, 1965). An animal born in a relatively mature state, such as the calf (Roy *et al.*, 1957) or lamb (Dawes and Mott, 1959), has a high rate of heat production from birth, like the pig. In addition, the calf and lamb have thick coats which conserve heat and so give them a substantial advantage over bare-skinned mammals such as pig and man.

C. HYPOTHERMIA AND RECOVERY

The body temperature of a new-born mammal falls immediately after birth. The extent and duration of this fall are determined by the species and the external conditions. The body temperature of a new-born pig often falls by 2–3° during the first 20 min. or so after birth, and then rises towards the mature level (Newland *et al.*, 1952; Pomeroy, 1953; Mount, 1959). The rise takes 1–10 days according to the ambient temperature. Although the new-born pig greatly increases heat production on exposure to, say, 5°, the rectal temperature nevertheless tends to fall if the piglet is alone and unprotected. The fall depends in part on body weight and age (Mount, 1961, 1963a) but there is much individual variation which cannot be accounted for in this way.

Other species undergo analogous changes, but the details depend on body size and maturity at birth. A new-born rat's body temperature falls several degrees when the mother leaves the nest exposed to an ambient temperature of 15° for 30 min.; but, if the nest is in a room at 28–30°, the difference between rats feeding from the mother, and those left exposed by the mother's absence, is not significant (Gelineo, 1959). The puppy, too, is thermally unstable at birth (Jensen and Ederstrom, 1955). By contrast, the temperature of a new-born guinea-pig remains at about 38° even if it is kept at an ambient temperature of 10°; but, if the ambient temperature falls to 6°, body temperature falls rapidly

to 16° and the animal may die (Gelineo, 1959). New-born rats, however, can be subjected to these low temperatures and still recover.

Adolph (1951) and McCance (1959) have discussed the way in which new-born animals can survive a much greater fall in body temperature than adults of the same species. Adolph found that the guinea-pig could survive cooling only to around 15°, whereas new-born kittens and rabbits could recover after experiencing body temperatures of 6°, and rats survived after having been as low as 0°. By any standards—open eyes, thermal insulation, feeding—the guinea-pig is more mature at birth than the other species mentioned. It is also a much better homeotherm, but this evidently entails a lower tolerance of cold.

D. EARLY EXPOSURE AND COLD-RESISTANCE

The conditions in which mammals are reared can have a considerable influence on their later response to cold. This is one aspect of a larger phenomenon: early exposure to slightly adverse conditions probably improves subsequent resistance, not only to cold but to other "stressors" (Levine, 1962; Hutchings, 1963; Schaefer, 1963). Early exposure of female mice to cold may also improve their reproductive performance (Barnett and Burn, 1966).

The rate at which thermoregulation develops in new-born rats depends on the temperature of the nest (Gelineo and Gelineo, 1951). Rats may be reared at nest temperatures below 10–12°. At the end of the first post-natal week, such rats have a higher oxygen consumption at 21° than at 30°; but those with a nest temperature of 23–23.5° do not respond in this way until about 10 days, and those with a nest temperature of 28–30°, only towards the end of the second week. If a litter of rats, with the mother, is exposed four times a day for 1 hour to 0°, the oxygen consumption at an environmental temperature of 29.5° is increased earlier than in controls (Capek *et al.*, 1956, quoted by Hahn *et al.*, 1961). Correspondingly, if rats are reared from birth with their mother at a temperature of 34°, the development of thermoregulation is delayed; but this delay does not occur if the animals are exposed to a temperature of 0° for 1 hour daily between the fourteenth and the eighteenth day after birth. Eighteen days is the time at which a homeothermic response usually develops. Hahn *et al.* (1961) suggest that the effects of a rat's early environment probably persist throughout life.

VIII. Some Problems

A. MULTIVARIATE ANALYSIS

Most of the observations we have quoted have been on animals suddenly exposed alone to moderate cold. The syndrome of cold

adaptation then includes increased heat production, improved thermal insulation, changed behaviour and altered proportions by weight of organs, tissues and substances. All these entail the operation of negative feedbacks which keep the core temperature and certain chemical features of the body at steady values. Among the feedbacks are those of the nervous and endocrine systems; but there is also intracellular regulation; and compensatory growth is controlled in ways which are still obscure.

A major problem of the immediate future is to analyse just how these many processes, hitherto examined piecemeal, interact and regulate each other. For this, more factual raw material is needed; but, once obtained, it will present problems of multivariate analysis which can be solved only by modern computing methods. The time has come when research programmes may be planned to provide material for computer analysis.

The need for these methods is increased by the temporal sequence of cold adaptation (Section II.C, p. 424). A change of environmental temperature does not merely require a resetting of the rates of a number of regulated processes: there is a series of stages, in each of which there are characteristic settings of, for instance, the rates of hormone secretion and enzyme activity.

B. GENOTYPE AND ENVIRONMENT

The seasonal changes, to which mammals in temperate and arctic regions are exposed, differ from the exposures used in laboratories: (1) they are gradual and fluctuating, and (ii) they are usually ameliorated by the protection of a nest and of huddling with companions. These differences, as Héroux has shown, can certainly influence the course of cold adaptation, even in laboratory rats. Moreover, the response to cold of a wild mammal may be different from that of laboratory strains of the same species (Héroux, 1963). Under genetical differences within species, two general types of effect have to be considered (Barnett, 1965a): (i) heterozygosis alone can confer superior cold resistance; (ii) selection of particular genotypes, in accordance with the demands of the environment, is inevitable in any large, heterogeneous population. Little is known about the detailed operation of either of these.

A more specific question is suggested by the work on wild and laboratory rats just quoted. If isolated wild rats were subject to more severe cold than those observed by Héroux, would their response more closely resemble that of laboratory rats to moderate cold? This sort of question arises also for other species.

C. ONTOGENY AND CROSSED RESISTANCE

Much work has been done on the development of homeothermy in young mammals, but remarkably little is known of the effects on later development of differing degrees of exposure in early life. This sort of question has so far been the concern more of students of behaviour than of physiologists. Early stimulation, involving exposure to cold, can influence later resistance to adverse conditions (Section VII.D, p. 465); it may also affect behaviour and maternal efficiency. The age of exposure is important, for there are sensitive periods in development, during which stimulation by hostile conditions produces more profound changes than at other times.

The multiplicity of the effects of early stimulation raises the question of the effects of exposure to one kind of adversity on resistance to others. For example, if laboratory rats have tourniquets on both hind limbs for 4 hours, most of them die after the bandages are taken off. Previous exposure to cold increases resistance to the hind limb ischaemia so produced; but the relationship between the two types of "stress" is not symmetrical, for previous ischaemia lowers resistance to cold (Schachter *et al.*, 1959; Stoner, 1963). An obvious difference between the two conditions is that cold-adaptation is a slow process which can leave the animal in good health, while ischaemia is not.

An attempt was made in the 1940s to construct a unitary theory of the response to a hostile environment. It was based, in part, on the increased activity of the adrenal cortex resulting from such diverse agencies as cold, infection and wounding (Selye, 1946). Today, adrenal and other endocrine effects are seen as only peripheral: attention is increasingly turned to the brain, especially the hypothalamus, as the source of all adaptive responses to adverse conditions such as cold (e.g. Ganong, 1959; Ganong and Forsham, 1960; Vogt, 1960). Quite separately, the studies of the consequences of early stimulation have led to the notion that, to be effective, stimulation has to be stressful, in the sense of activating the hypothalamus and the pituitary and other endocrine organs (Levine, 1962).

Accordingly, general questions which need to be investigated by experiment now include the following: (i) To what extent does adaptation to one kind of adverse conditions increase or diminish resistance to others? (ii) What are the changes—neural, endocrine and so on—which produce crossed resistance or sensitization? (iii) To what extent does age at exposure to unfavourable conditions influence the later consequences of the exposure? (iv) When there is a prolonged improvement in resistance, what intracellular changes in nervous and other tissues are responsible?

D. PREGNANCY AND MATERNAL EFFECTS

The normal life history of a female mammal includes, in pregnancy and lactation, states which, like exposure to cold, raise the rates of flow of matter through the body. Two general questions are: (i) to what extent does adaptation to cold influence maternal efficiency? (ii) to what extent does pregnancy (or lactation) influence resistance to cold? These questions would have to be made more specific to provide a basis for an experimental programme. First, there is the matter of the precise temperature: what is "cold" to a laboratory mouse would not necessarily be so to a polar bear, *Ursus maritimus*. Second, temperatures which allow survival sometimes preclude breeding: does prior adaptation to cold lower the temperature at which, say, a rat or mouse can reproduce? Third, when a mammal does breed in an ambient temperature much below the optimum, how do the physiological effects of cold and pregnancy (or lactation) interact?

After some pioneering work by Parkes and Brambell (1928), remarkably little work was done on the reproduction of mammals in cold environments for a quarter of a century. But we now know that even laboratory mice can breed at freezing temperatures, given nest material (Section VI, p. 453). Hence a large and almost new area of study of cold adaptation in mammals has been opened. The questions which have consequently to be asked concern not only maternal performance in a hostile environment but also the effects on the young of cold-exposed females. In general, the body weight (for example) of a mammal reflects the maternal genotype (and the environmental influences which have acted on the mother) up to birth or even to weaning; after this, the genotype of the offspring, and the action of the environment in which it is living, become effective (McLaren, 1960). But maternal influences may still be evident in the adult, for instance in the reproductive performance of females. Hence, effects of exposure to cold can be passed, by non-genetical means, to a second generation (Barnett, 1961, 1965a); but the scope of the information so transmitted, and the number of generations which can be measurably influenced, have still to be discovered.

IX. Summary

Mammals are homeothermous in the sense that their deep body temperature remains steady while the outside temperature changes. Thermal neutrality is the range of temperature at which resting metabolism is minimum. The critical temperature is that at which heat production increases, and so maintains body temperature, despite greater heat loss from the surface.

Insulation. The greater the insulation, the lower the critical temperature: the range is from about 30° for small tropical mammals, to -40° for arctic species. Many mammals grow thicker hair in winter, and some put on more fat. All mammals which have been tested, regardless of insulation, can increase heat production when stimulated by cold. This increase depends on the thermal demand of the environment, or the total heat loss from radiation, convection and conduction.

Immediate Response to Cold. When a mammal is suddenly moved to an environment well below the critical temperature, its first response is peripheral vasoconstriction (which reduces loss of heat) and shivering (which increases heat production). There is also an immediate increase in the secretion of hormones by the adrenal medulla. There follows greater activity by the pituitary, thyroid and adrenal cortex. The metabolic roles of these hormones are not yet clear.

Metabolism. If the cold persists, shivering ceases but extra heat production is still maintained. The development of this "non-shivering thermogenesis" is accompanied by a sequence of changes in the enzymic activities of the muscles, liver and other organs. The cold-adapted tissues are more responsive to noradrenalin.

Eating. In winter, or on experimental exposure to cold, a mammal, even up to the size of a large dog, eats more. But intake is not adjusted to brief fluctuations of temperature. Cold-adapted animals probably also utilize their food more efficiently. The extra food evidently need consist only of carbohydrate, but the optimum diet for severe cold is not known for any species. Rodents, given a choice, take extra carbohydrate rather than protein or fat.

Behaviour. Mammals are less active in a cold than in a warm environment, especially before cold adaptation is complete. Nest-making species make better nests, and select warm surfaces to sit on; huddling by species ranging from mice to pigs can be an important means of conserving heat. Efficient nest building may require a gradual learning from experience. Rats and pigs can learn to push a switch to turn on a source of heat.

Growth. Heat conservation is aided by an increase in body weight in a cold environment, but such an increase rarely, if ever, occurs in an individual mammal on exposure to cold. Laboratory mammals usually lose weight on exposure to about 4°, but young ones may later restore it. Exposure to cold in early life may result in permanent stunting; but later exposure can have an opposite effect. Selection for resistance to cold, over several generations, can result in a genetically determined increase in body weight.

Body shape may be influenced by the temperature of the environment

during growth. The appendages, especially the tails of rodents, are shortened by cold.

Adaptation to cold is accompanied, at least in laboratory animals, by the enlargement of organs that do more work, namely, heart, gut, liver and kidneys, and thyroid and adrenal glands. In addition, hair usually grows longer during prolonged exposure.

Changes in body weight, or in the weights of organs, only crudely reflect alterations of function. Organs can become more efficient without increase in size.

Body Composition. On sudden exposure to cold, there is a marked loss of adipose tissue and there may be loss of muscle. These can sometimes be made up after shivering has ceased, but living in a cold environment may entirely prevent the deposition of the amount of fat present in a warm environment. "Brown fat" is a special type of adipose tissue, even more labile than white fat, which produces much heat on sudden exposure to cold. It is important in young mammals. Both types of adipose tissue undergo enzymic changes, evidently adaptive, during prolonged exposure.

Other chemical changes in cold-adapted small mammals include an increase in the proportion of water, and a decline in nitrogen, calcium and collagen.

Reproduction. Usually, mammals stop breeding in the cold season. This may be due to shortage of food, rather than low temperature. Even laboratory mice, given excess food and bedding, can breed in an environment at -3° . In them, low environmental temperatures delay reproductive maturity in the female, lengthen the oestrous cycle, and postpone the birth of the first litter. The effect of cold on reproductive performance depends on whether the animals have been transferred to a cold environment, or reared there. Mice transferred from 21° to -3° (with bedding) as young adults are less fertile; but their offspring are usually less fertile still. The third generation may, however, partly recover. The full scope of such maternal effects has still to be determined, but there is evidence of the possibility of a non-genetical, cumulative adaptation to cold over several generations.

Ontogeny. Small mammals, and some large ones, are virtually heterothermous at birth, but some newborn artiodactyls, at least, are homeothermous. The newborn laboratory rat has some capacity to increase heat production if the outside temperature falls slightly, especially just after a meal; and the guinea-pig, *Cavia*, has greater powers of thermoregulation. Larger mammals respond more effectively: the hairless piglet, *Sus*, can shiver virtually at birth. There is a rapid change towards the adult form of homeothermy during the first days or weeks. Newborn mammals can survive degrees of hypothermia which would kill adults.

Early exposure to moderately adverse conditions, such as cold, can probably improve resistance to stressful conditions in later life.

Problems. The many, changing processes, reflex, behavioural, enzymic and "trophic", involved in adaptation to cold, present problems which can be solved only by multivariate analysis.

Genetical problems include the relationship of hybrid vigour with resistance to cold, and the differences between wild and laboratory varieties of the same species.

Little is known about the effects of early exposure to cold on subsequent development. Exposing an adult to cold can improve its resistance to other adverse conditions, but the mechanism of this crossed resistance (and of the opposite, crossed sensitization) is not known.

A complete account of cold-adaptation in mammals requires information on the effects of cold on reproduction, and on the characteristics of the young of cold-exposed females.

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