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The biochemistry of natural fasting at its limits

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Abstract. There are several groups of animals that are adapted for extremely long duration fasting as part of their reproductive cycle. Penguins, bears and seals routinely fast without food or water for months at time. However, they do not 'starve', as the biochemical implications of starving are very different from those of successful fasting. There are distinct biochemical adaptations in lipid, carbohydrate and especially protein metabolism that allow these animals to survive. It appears, at least for penguins and seals, that the duration of the fast may be limited by changes that occur in biochemical regulation near the end of the fast. In all of these species, the biochemistry of fasting and the ecological and behavioral demands of their breeding cycles are closely interrelated.

Key words. Starvation; penguins; seals; marine mammals; bears.

There are many factors that are involved in the regulation of food intake. In healthy humans for example, food consumption on a day-to-day basis can be proximately regulated by social factors, activity levels and hormonal control of appetite, all of which are ultimately linked to providing homeostatic regulation of metabolic biochemistry[23,49,54,65]. There are animals, however, that are adapted to withstanding very long periods with neither food nor water. Some of these fasting periods are related to a lack of available food while others are part of the natural history of the species. For example, the marmot *(Marmota flaviventris)* can fast for up to 3 weeks in the winter when food is lacking[22] while the northern elephant seal *(Mirounga angustirostris)* can fast for up to 90 days as part of its breeding cycle[18,34]. In all of these cases of natural food deprivation, however, there is a critical distinction between fasting and starvation. The fasting animal is adapted to maintain a level of metabolic homeostasis so that critical organ function is maintained. Starvation, however, is a state in which homeostatic control is lost and critical organ function becomes compromised[67,69,74]. Thus, an animal may 'starve to death' when deprived of food but an animal that naturally fasts would not 'fast to death'. In this review we ask the question: Does extended natural fasting ultimately reach the point of starvation and if it does, what role might this metabolic switch play in the natural history and ecology of the species?

This review focuses mainly on the metabolic biochemistry of long duration fasting in normothermic mammals and its relationship to the ecology of the species. It deals with penguins, bears and seals, species in which extended fasting and reproductive behavior are closely linked. There are many species that routinely endure short periods of fasting in the order of a week or less but do not enter into long periods of food deprivation. There are excellent works available on the hormonal control of appetite and the impact of torpor and/or hibernation on fasting biology[23,30,41], and these issues will not be discussed here.

Non-fasting adapted species

For obvious medical reasons, a great deal of work has been carried out on the need for food in humans and fasting/starvation has been modeled extensively with laboratory animals. Some humans have been able to survive without food for over 12 months[68], but long-term fasting is not a routine part of human behavior. The basic elements of fasting and starvation have been defined in humans and animal models and are described in detail in a series of reviews[9,10,24,25,29,31,39,74]. The literature in this area of human fasting/starvation is so extensive that we have summarized the field using the above general reviews with specific references only to detailed points of interest.

During the first few days of food deprivation, termed Phase I, the hepatic glycogen reserves are almost completely utilized as the body defends circulating glucose levels. Glucose is a critical fuel for the central nervous system (CNS) and its circulating concentration is tightly regulated. During this initial phase of fasting, the mobilization of stored lipids is activated as the body starts to switch to fat oxidation and reduce protein catabolism. The overall metabolic rate begins to decline at this point and, in humans, can fall to less than 50% of the non-fasting rate. It should be noted that in extreme fasting, humans reduce body movements to a minimum.

Phase II of fasting begins soon thereafter and involves the increased oxidation of lipids, the production of ketone bodies and the partial sparing of proteins. The increased demand for lipids is required to provide metabolizable energy for the body. However, the demand for CNS fuel is not changed during fasting and the body has presumably depleted its circulating glucose supply. How is the energy demand of the CNS met? Lipids cannot cross the blood-brain barrier, but ketone bodies, a product of lipid catabolism, can cross the barrier and act as a fuel source to the brain. Consequently in the non-fasting adapted species, both circulating lipids (as non-esterified fatty acids; NEFA) and ketone bodies increase in concentration in the blood. Unfortunately, the high production of ketone bodies also alters the acid-base balance and a state of metabolic acidosis (ketosis) may develop. Ketone bodies are not the only source of fuel for the CNS, however, as protein degradation to amino acids provides the precursors for gluconeogenic production of glucose. Thus, during Phase II fasting, ketones from lipid utilization and glucose derived from protein provide energy for the CNS, while oxidation of fat provides the energy for the remainder of the body. Figure 1 summarizes these biochemical changes in non-fasting adapted species.

Superficially, complete starvation sounds like an ideal method to lose fat and thus, body weight. Yet it is not considered a healthy option for most people. Why? The answer lies in the rate of protein utilization. While protein catabolism is decreased during fasting, it has not stopped. Thus, after a long Phase II, the body may still have an adequate supply of lipid to burn, but protein from skeletal muscle will start to become limited. Unfortunately, cardiac muscle is one of the first sources of protein that is utilized as the body catabolizes protein to amino acids in order to supply CNS fuel via gluconeogenesis[69]. Thus, a person who still has a very high 'fat index' can suddenly die due to protein wasting in the cardiac tissue. Apparently, the body does not recognize the excessive loss of protein and there is no signal to end the fast. In some fad diets, liquid protein supplements were promoted as an energy source during long fasts. Unfortunately, this protein was not of the correct nature to provide the essential amino acids for gluconeogenesis and cardiac muscle wasting still occurred. A significant number of people died on these liquid protein diets.

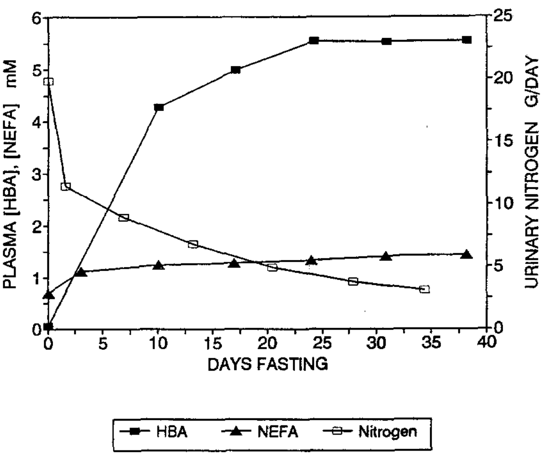

Figure 1. Changes in plasma concentrations of HBA and NEFA and total urinary nitrogen excretion during fasting in humans. (Source: modified from Linder 1985.)

Stage III, or terminal starvation, occurs when 30–50% of the body protein has been wasted. At this point, lipid utilization falls, circulating ketones decline and the subject is in serious risk of literally starving to death. Other organs in addition to cardiac tissue are compromised at this point. For example, the kidney can be in risk of renal failure due to accumulation of uric acid[32]. Recovery by re-feeding from this stage is a long and difficult process and can take up to a year in humans even under close medical supervision[9].

Clearly, the entrance into stage III terminal starvation is not an ecologically sound approach to long-term fasting. If the biology of the species requires extended periods without food, the most reasonable solution would be to prolong Phase II, thereby sparing body protein as long as possible and to end the fast before Phase III begins. This basic solution, with interesting modifications, is the pathway utilized by the fasting adapted species such as penguins, bears and seals.

Fasting adapted species

Penguins

Of all the birds, the penguins naturally fast the longest and are capable of going without food or water for 150 days[15]. The natural history of fasting and its biochemistry have been studied most extensively in the emperor penguin *(Aptenodytes forsteri)*, although other species, such as king penguins *(Aptenodytes patagonica)*, are also capable of surviving long periods without food[15,27,36]. Long-term fasting for these birds is linked to their breeding biology. The emperor penguin lays an egg while brooding on the frozen sea ice of the Antarctic in mid-winter. After the female lays the egg, she passes it to the male who incubates it while the female travels back to the sea to feed. The female is at sea for about 2 months before she comes back to relieve the male who has gone the entire period with no food. The female returns about the time that the egg hatches and she feeds the chick with regurgitated food while the males leaves the pair to feed at sea. Counting the initial time that it took to reach the breeding grounds, the male emperor penguin has now fasted for about 4 months.

If the female does not return, what options exist for the male? One possibility is that he continue to fast and hatch the chick. Males produce a 'curd' to feed chicks, but only enough for about a week or two[27]. Ultimately, the male will abandon the young and go to sea to feed if the female does not return. However, it is about a 100-km walk for the male bird to reach the open water. There must be some way that the male balances the need to protect the young with the limits of its own fasting ability. If the male waits too long, would it have the energy needed to reach the water? Studies have shown that the break point for the male correlates to fundamental shifts in metabolic biochemistry. Thus, for the emperor penguin, feeding behavior, the rearing of the young and the survival of the adult depend critically on biochemical/ecological interactions.

Like the non-fasting adapted species discussed earlier, the penguin shows three phases of fasting[26, 27, 37]. During Phase I, rapid changes in metabolism occur as the bird defends body glucose, prepares to mobilize fat and decreases protein utilization. This phase begins as soon as the birds leave the open ocean and head 'inland' onto the frozen sea ice to their breeding areas. By the time that they reach their rookeries, they are in fasting Phase II. This protein sparing stage is extremely long and continues until the male is either relieved, or abandons the youngs, at about 120 days. During this phase, there is a marked reduction in protein utilization. Ketone bodies and NEFA increase and the bird loses weight in a stable and linear manner. In Phase II, protein accounts for less than 5% of the energy utilized while fat makes up the remainder. Ketone bodies increase about four times in these birds to approximately 1.5 mM and NEFA increase less than two times to just over 1.0 mM. There is also evidence of selective mobilization of stored fatty acids by the penguins during this period[27]. The birds are relatively immobile at this time and only move about 30 m/day in an effort to conserve energy. By dropping their metabolic rate, these birds effectively extend their fast by 3–4 times[27].

Under normal conditions, when the female returns to relieve the male, has he reached his limits of fasting? Alternatively, what happens at 120 days into the fast that alters the birds behavior and makes it abandon the young and return to sea if the female does not return? By capturing birds and preventing them from leaving, researchers have been able to monitor the biochemical changes that occur at the break point. Studies have shown that the behavioral shift occurs approximately at the entrance into stage III fasting[26]. At about 120 days, protein utilization increases rapidly, probably because the lipid stores have reached a critically low level. At this point, the bird has only about 20% of its initial fat reserves left. However, given the evidence for selective utilization of NEFA, the key point may not be the absolute amount of lipid reserve, but rather the type of lipids that remain. The reduction in fat oxidation decreases circulating NEFA and ketone bodies. Thus, the increase in protein utilization is necessary not only to provide total body energy, but also to provide amino acids for gluconeogenesis so that the CNS will have a fuel source as the ketone bodies decrease. The significant increase in protein utilization drives up circulating blood uric acid, a waste product of protein catabolism. A schematic view of these shifts is shown in figure 2. It is interesting that the average NEFA concentrations are not high (about 1.0 mM) and that ketone body concentration is relatively low. This suggests that ketosis is not a problem in these birds, although the level of ketone bodies is sufficient to provide a fuel source for the CNS.

Once the male bird reaches this late point in its fast, it must still travel a great distance to get to sea to re-feed. Apparently the remaining amount of lipid reserves and protein are enough to get the animal to the water without the penguin starving to death. Phase III fasting is not a terminal pathway in these birds as they re-feed successfully and restore their body condition both in nature and under experimental conditions. There are probably some birds that do not make it to the water and die due to starvation. The biochemistry of re-feeding is poorly understood, however, and there are no current models suggesting why some species can easily recover from long fasting and others do not.

Fasting biochemistry in penguins has only been studied for less than 20 years, but there are many excellent research articles and reviews that cover this interesting field[13, 14, 26, 27, 35, 36, 38, 66].

Bears

The biochemistry of long-term fasting in bears is similar to penguins and also involves clear relationships to ecological requirements. It is important to note that fasting in bears is not true 'hibernation'. While bears may den

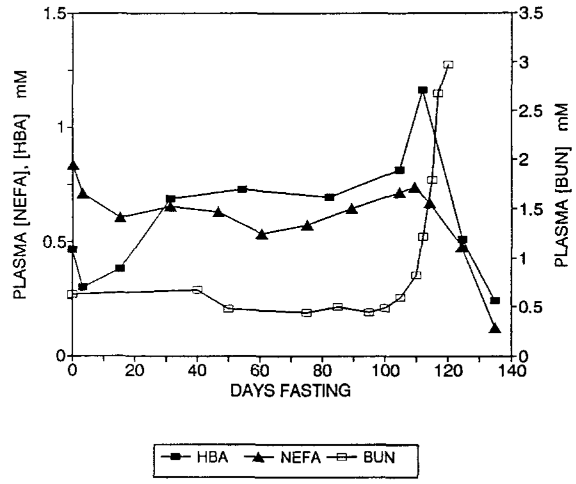

Figure 2. Changes in plasma concentrations of HBA, NEFA and BUN during long-term fasting in emperor penguins. (Source: modified from Groscolas 1986 and Robin et al. 1988.)

and sleep during most of the winter, they are not hibernating in the sense of dropping body temperature to the low levels seen in small, hibernating rodents. Rather, their body temperature drops only a few degrees and the bears remain alert.

Most fasting work on bears has been conducted on the black bear *(Ursus americanus)*. This species dens from October until April. During this time the bears become essentially a closed system as they do not eat, drink, urinate or defecate. Body temperature drops about 5°C and heart rate declines by 80%. Yet, in spite of this torpid state, cubs are born in January and suckled through the remainder of the fast. During this time, the metabolic rate of the fasting bear is only 67% of normal, about 4000 kcal/day[42,43,45,46].

Like the fasting penguins, the regulation of biochemical pathways is of critical importance to the fasting bear. The denning bear has a very low respiratory quotient (RQ) of around 0.60 indicating that not only is it burning essentially only fat but that it must also be recycling carbon at some point. Thus, the oxidation of fat provides most of the total body metabolic energy. However, there is still the need for fuel for the CNS. Like all mammals, the hepatic stores of glycogen only last a few days after the beginning of a fast. In the bear, the glycerol produced from the breakdown of lipids is probably the main substrate for gluconeogenesis[2]. The bear also produces ketone bodies during fasting as a fuel source for the CNS and ketones increase by ten times over fed levels. In non-fasting adapted species, such as man, ketones can increase by 500-fold. Interestingly, in the bear, fasting ketone levels reach only 0.2 mM as contrasted to levels exceeding 5.0 mM in fasting humans. Thus, the bear avoids the metabolic acidosis caused by excessive concentrations of ketone bodies. The final concentration of ketone bodies in the bear is only $^1/_5$ to $^1/_6$ of that level found in fasting emperor penguins and only $^1/_{25}$ of that found in fasting king penguin chicks. In the marmot, mentioned earlier, ketone body concentration becomes quite high and is considered to be a trigger for arousal[4].

What pattern of protein metabolism occurs in the fasting bear? The gluconeogenesis provided by glycerol metabolism probably provides most of the glucose needed for CNS metabolism. However, actual protein turnover increases 3–5 times with the increased amino acid turnover going back into protein synthesis, glucose and lipids. The result is that net nitrogen production declines by 80%. However, it is also known that the bear produces no urine during this time. What happens to the urea nitrogen that is still minimally produced by protein metabolism? Urea turnover in the animal increases by 2–10 times but total blood urea nitrogen (BUN) concentration declines[45] and the minimal urea that is produced is completely re-absorbed from the bladder. Thus, no nitrogen is excreted by the bear for months, lean body mass remains constant and may actually slightly increase[40,47]. There is no other mammal known that can completely conserve body protein during fasting.

It is intriguing to ask what determines the length of the fast if the bear can completely recycle nitrogen and is in no danger of terminal protein wasting. In these animals, the determining factor is probably a combination of the total amount of fat available to provide basic metabolic energy and the hormonal/behavioral/ecological signals associated with circannual rhythms and the coming of spring. There is some evidence that the denning period is under hormonal control[43]. Once the bears come out of their dens, they still do not eat for over a week[42]. Certainly, for the female bear, the increased energetic demands of growing cubs would also limit her ability to fast. The biochemical regulation that allows the female bear to completely fast and simultaneously suckle the young must be very interesting, but has not been explored. It appears that the bears must be metabolically prepared to fast, because if they are experimentally fasted during the summer, they respond just like any other mammal and utilize excessive amounts of muscle protein[47].

There has been a great deal written about fasting in bears and the reader is referred to these reports for additional information[20,28,30,44,48,59].

Seals

Spontaneous long-term fasting is an integral part of the natural history of phocid seals. Breeding, giving birth and nursing pups, and the annual molt all require extended periods of time on land and seals undergo voluntary periods of prolonged fasting two times per year to participate in these activities. In polygynous breeding systems, in which the breeding males compete for and hold territories, males may remain on the rookery fasting for up to 90 days[33]. Also, phocid seals are characterized as having a short but intensive lactation period during which the female remains on land and fasts while nursing her pup. The pups are weaned abruptly and in many species the young also undergo an extended post-weaning fast before leaving for sea to feed[64]. In most cases there is a considerable energy expenditure associated with these activities (i.e. active combat to hold harems, breeding, molting or nursing a pup) and adults may lose 36–42% of their original body mass during this time[17,21].

The length of these fasts vary a great deal between species. In some phocids, such as the hooded seal *(Cystophora cristata)* this fast can be as short as 1–2 weeks (the hooded seal female weans her pup in 3–5 days[5,6]), whereas northern elephant seals nurse a pup for 25–30 days in addition to fasting 1–2 weeks prepartum[63].

In contrast to penguins and bears, seals remain relatively active throughout their periods of food deprivation. Although seals sleep a great deal during the day, they are very active when awake. Adult male elephant seals engage in combat the entire time that they hold a territory, in addition to the energy expended mating females in their harem. Pups are also active throughout their post-weaning fast making daily forays to the water. Females are relatively stationary within the harem once they give birth, although they have the additional energy drain of nursing a pup. But even when faced with this continued energy expenditure, seals are still able to minimize the loss of lean body mass as the fast proceeds. Within the first 2–4 weeks of the fast, the rate of mass loss decreases by approximately 50%, and then remains relatively stable and low throughout the rest of the fast[52,60,73]. This decrease in rate of mass loss is primarily due to a decrease in total body metabolism during the fast. Metabolic rate decreases as the fast progresses in many species both on a whole body basis, and also when corrected for decreasing body size and changing body composition[52,60]. This adaptive depression of metabolism can be reversed when seals are re-fed following a long fast[60,71]. Thus, seals can increase their fasting time by decreasing metabolic rate, but they still face the problem of protein wasting and vital organ damage.

As seen in penguins and bears, prolonged Phase II fasting, with the sparing of body fat and particularly body protein, is the key to enduring extended periods of fasting during the breeding season and the molt in seals. How do seals accomplish this crucial sparing of body proteins? A substantial decrease in the blood urea nitrogen levels in the blood is seen within the first week or two of the fast indicating decreased protein degradation[1,18]. Urine output also decreases significantly during the fast due to the decrease in nitrogenous wastes[1,62]. During this time the proportion of protein reserves being utilized also decreases, both on an absolute and proportional mass loss basis[62]. Protein mass loss contributes 14% to the total energy demand during the first 2 weeks of the fast but this proportion decreases to 2–6% by the end of the fast[50,52,58,62,72].

In seals, like other fasting adapted species, NEFA provide the majority of the body's metabolic energy needs during long-term fasting. Increases in plasma concentration and turnover of NEFA are seen during the fast in both grey seal *(Halichoerus grypus)* and elephant seal pups[12,51]. These circulating levels (up to 2.5 mM) found after 1.5–2 months of fasting were higher than any values previously found in marine mammals[12]. There is evidence that seals can selectively utilize reserves from different parts of the body (i.e. core proteins or fats vs blubber tissues) during different stages of the fast[55,72,73]. This could be important for ensuring an adequate blubber layer for thermoregulation when the animals go to sea to feed at the conclusion of the fast. Bryden and Stokes[8] suggest that long-chain fatty acids (chain length > C_{18}), are the main source of fuel during the fast in both adult females and pups whereas a separate group of fatty acids (16 : 0) are indicated in transfer of lipids from mother to pup for build-up of the neonatal blubber layer.

Ketone bodies (HBA) accumulate during the fast in both elephant seals and grey seals, and then decline rapidly near the end of the fast[11,51]. The increasing HBA levels as well as high turnover suggest that ketone bodies contribute significantly to the energy requirements of seals during long-term fasting. The declines near the end of the fast mimic those seen in penguins just prior to departure from the ice. It should be noted that HBA concentrations never reach levels that would affect the acid-base balance of the blood, as is often seen in non-fasting adapted species. Like penguins and bears, seals never become ketotic despite months of fasting.

Evidence of Phase III fasting in seals has been inconclusive. The predictable peak in ketone body concentrations near the end of the fast in fasting seal pups would suggest that Phase III had been reached. However, only two studies have shown increases in nitrogen excretion following the period of protein sparing in seals[52,72]. It may be that under normal voluntary fasting conditions Phase III fasting or terminal starvation is never reached. In penguins, evidence of Stage III fasting was only seen in birds that were forcibly fasted past their natural departure times. Similarly, seals may leave the breeding beaches before initiation of stage III. The initiation of increased protein catabolism in penguins occurs when birds have diminished body fat reserves to about 10% of total body mass. When elephant seal pups leave for sea, they are still about 45% fat. Do seals ever enter a Phase III situation when endogenous lipid stores have not been exhausted? And if the end of the fast is not determined by the remaining energy reserves available, why do seals leave the beach? These questions will remain until we better understand the biochemistry of seals at their limits of fasting. Figure 3 graphs some of these key metabolites in fasting seals.

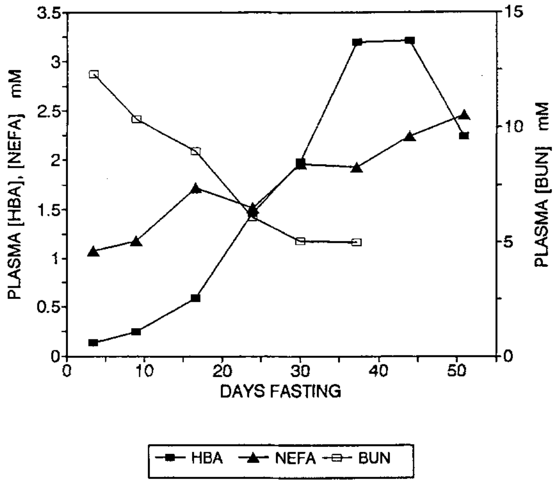

Figure 3. Changes in plasma concentrations of HBA, NEFA, and BUN during long-term fasting in grey seals and northern elephant seals. (Source: modified from Nordoy and Blix 1991 and Costa and Ortiz 1982.)

Present and future studies with marine mammals

Recent experiments have focused on monitoring the changes in plasma concentrations of BUN, NEFA, and HBA in elephant seal pups near the end of their post-weaning fast[61]. As in previous studies, no evidence of ketosis was found at any time during the 12-week fast. HBA levels always remained below 2 mM and rarely rose above 1 mM. However, unlike previous studies that showed a distinct decline in HBA levels after the peak, the animals in this study showed great individual differences in HBA concentrations after this point in the fast. This more complicated metabolic scenario may simply reflect the longer sampling regime of this latest study. However, there is some evidence that body mass of the seals may alter the biochemical patterns seen during fasting. In previous studies, the range in the body mass of animals studied was small. In contrast, the range of body mass in this study was quite broad and one extremely large pup showed very low HBA levels until 10 weeks into the fast and then only slowly increased plasma concentrations, even after 12 weeks. Figure 4 shows how this is different from patterns seen in pups of average mass. Considering the importance of maintaining an adequate blubber layer for thermoregulation once at sea, even a pup with 45% of its body mass remaining as blubber at the end of the fast may be limited in lipids that can be catabolized for energy. However, there was nothing to indicate that utilizable lipids were exhausted. NEFA concentrations increased gradually up to about 55 days, and then the frequency and magnitude of changes varied between individuals. There was certainly no evidence of consistently lower levels of NEFA available at the limits of the fast, or in smaller animals.

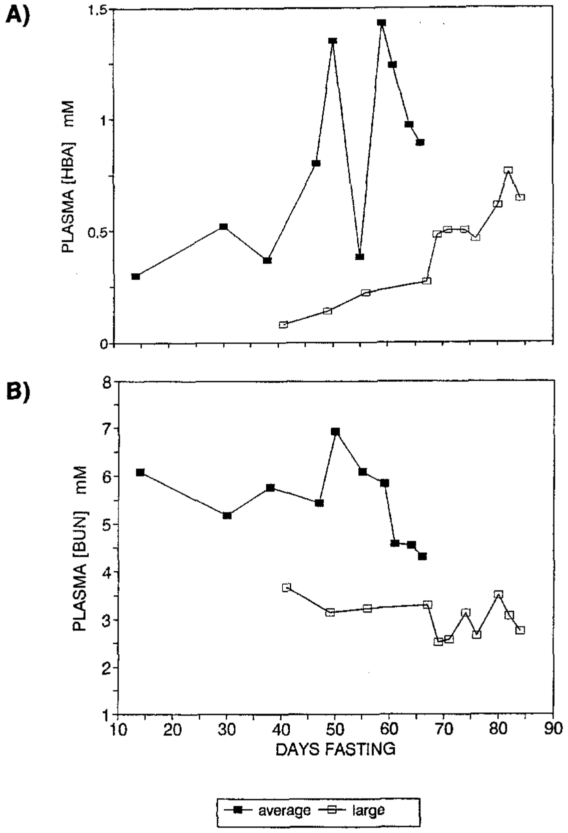

Figure 4. Changes in plasma concentrations of HBA (A) and BUN (B) during the postweaning fast in northern elephant seal pups. Mass of the average pup was 95 kg at 40 days fasting. Mass of the large pup was 156 kg at 40 days fasting.

It is obvious that these pups were still in a fasting adapted state even after almost 3 months of abstinence, as opposed to the starvation state that would be evident in most mammals. BUN concentration decreased early in the fast and remained constant and low. Only 3 of 20 pups showed increases in BUN concentrations near the end of the fast. However, in all three cases, BUN levels decreased again immediately after this peak. As mentioned earlier, two other studies have found evidence of increased protein catabolism at the limit of fasting in grey and harp seal pups[51, 72]. Overall, there was no clear evidence of entry into stage III fasting in northern elephant seal pups, despite 12 weeks of voluntary fasting.

Most studies of fasting biochemistry have focused on young seals particularly during the post-weaning fast. These animals can deal with extended fasts of up to 3 months by modifying their metabolism and particularly by sparing protein reserves. But how does an adult female effectively fast and ration body reserves when she is faced with the additional energy drain of weaning a pup? Recent work on northern elephant seal females suggests that nursing mothers may alter their fasting biochemistry in a different manner than fasting pups. For example, by the end of the fast during the lactation period, plasma NEFA levels in females far exceed those found in any other marine mammal[70], yet are very low during the fast associated with molting[12].

Very little work has addressed fasting in other marine mammals, such as whales, walrus or fur seals and sea lions. In the otariids (fur seals and sea lions), only breeding males undergo extended fasts in association with breeding. Adult males will compete for and hold territories on the breeding rookeries and will fast for several weeks or months, depending on the species. In contrast to phocid seals, otariid females have developed a breeding system in which they alternate short suckling periods on shore with foraging periods at sea. The longest fast lasts 1–2 weeks post-partum before the first foraging trip to sea. Pups are left on the rookery during this time and therefore also undergo alternating periods of nursing and fasting. Changes in metabolic biochemistry during any of these fasts in males, females or pups are not well known and have only recently been studied[7].

There are many aspects of fasting biology in phocid seals that could not be included here. The reader is referred to the following references for a more complete understanding of fasting in seals[3, 16, 17, 19, 53, 56, 57].

Conclusions

By comparing the non-fasting and fasting adapted species, several interesting conclusions are drawn concerning relationships between feeding and natural behavior. First, and most obviously, despite the ability of non-fasting adapted species to survive without food for very long time periods, this behavior is not a routine part of their natural history. The metabolic and physiological consequences of food deprivation in these groups are severe and even re-feeding is complicated. In humans, long fasts are only safely undertaken under medical care. There simply is no ecological strategy for fasting in these groups...it is an emergency response that is utilized for survival under extreme circumstances.

Second, the biochemical *pattern* that is associated with food deprivation is similar between fasting and non-fasting groups, but vastly different in magnitude. That is, in general, metabolic rate and protein utilization decline, fat oxidation increases and gluconeogenesis and ketone body production provide fuel for the glucose dependent tissues. Among the fasting adapted species, however, the protein sparing phase is extremely efficient, nitrogen wastes are minimal and ketone bodies do not accumulate to levels that induce a metabolic acidosis.

Third, the fasting adapted species appear to have tied their natural behavior to the limits of their ability to manipulate protein metabolism. That is, the penguins and seals appear to end their natural fasts just before increased protein utilization would become necessary. There is no reason to suspect that seals or penguins could survive severe protein wasting any better than a human. The difference is that the routine natural history of their fasting habit breaks the fast before they achieve that level. The bears have completely negated problems with protein loss and could, in theory, continue fasting indefinitely if protein wasting were the only criterion for ending the fast.

We conclude that fasting, as part of the natural life history cycle of penguins, bears and seals, is a process that has been modified to allow a precise balance between biochemistry and ecology. The biochemical changes that occur during the fast appear to alter fasting behavior and provide some type of signal appropriate for ending the fast. Conversely, the ecological and behavioral requirements of the species are facilitated by their ability to fast. Thus, for these fasting adapted groups, ecology, behavior, physiology and biochemistry come together to form the *biology* of fasting.

Acknowledgments. Support for this work was provided from a University of Alaska Faculty Grant Award to M. Castellini.

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