Ratio of Serum Urea to Serum Creatinine in Wild Black Bears

Abstract. *In winter, the ratio of serum urea to serum creatinine is 10 or less in denning female and male bears. In midsummer it is 22 or more, similar to that of other mammals. However, in late summer and early fall, while food is available, the urea-to-creatinine ratio approaches or becomes 10 or less. The low value of this ratio appears to indicate the biochemical state of hibernation, and many bears are in this state weeks before they den.*

Bears are, perhaps, the most successful at starving of any mammal. At near normal body temperature (35°C), burning an estimated 4000 kcal/day, they can go for 3 months or longer without food or water (*1*). Under similar conditions, the human being can live only for days. During denning—a period that represents a state of hibernation (*2*)—bears do not urinate or defecate.

Important to the physiologic and biochemical adaptation of the bear during denning is control of urea metabolism, so that uremia and dehydration do not occur (*3*). Studies of bears in captivity have shown that the concentration of serum urea declines in winter (*3*). Associated with this change is an increase in serum creatinine (*3*). The net effect of these changes is a reduction in the ratio of serum urea to serum creatinine (U/C) from normal levels, above 25, to values less than 10 (*3, 4*). Some of the biochemical reactions necessary for control of urea metabolism have been summarized (*1, 5*). In mammals there are few, if any, instances where such low U/C ratios are achieved normally. Since bears that cannot hibernate fail to achieve this low ratio (*1, 6*), it must reflect the state of hibernation.

Preliminary studies in 1981 in Colorado indicated that similar changes in U/C occur in wild female and male bears while they den (*5*). An unexpected finding of these initial studies was that U/C in some bears had reached denning levels in late summer and early fall, weeks before the animals denned. A complicating feature of these studies was that in 1981 food was scarce, and this could have led to the low U/C values. However, after two subsequent years of study, during which food was plentiful, similar changes in U/C occurred. Many female and male bears showed values of 10 or less in late summer or early fall, weeks before they denned. Some of the female bears were pregnant, but their U/C ratios were also decreasing or in the low ranges. Considering that there are few mammals, if any, with similar documented U/C values of 10 or less, we propose that the low value of U/C is a biochemical indicator of the hibernation state. It can be achieved while food is available. Furthermore, sex and reproductive state do not influence the response.

Our 3-year study of the changes in U/C in Colorado wild bears began in the winter of 1981 and ended in the fall of 1983. The investigation was performed in the Black Mesa–Crystal Creek area in west-central Colorado. The study area has three major vegetation associations in elevational bands. At the lower elevations (2235 to 2330 m), a mountain shrub community dominated by Gambel oak (*Quercus gambelii*) and serviceberry (*Amalanchier alnifolia*) is most common. Extensive stands of chokecherry (*Prunus virginianus*) can be found throughout the upper reaches of this association. Above the oakbrush, at elevations between 2330 and 3330 m, are large aspen (*Populus tremuloides*) forests. Chokecherry thickets are often found at a boundary of these lower associations. At higher elevations mixed Engelmann spruce (*Picea engelmanni*) and fir (*Abies concolor* and *A. Lasiocarpa*) stands predominate. Mixed within the aspen and conifer forests are large meadows, once nearly pure Thurber fescue (*Festuca thurberi*), but now a mixture of seven to ten grasses, with significant number of geranium (*Geranium fremontii* and *G. viscosissimum*) and rabbit brush (*Chrysothamnus parryi*).

During the 3-year study, a total of 76 blood samples were obtained from 27 female and 21 male bears. During the two winters of the study, ten of the females had litters. Bears were captured with Aldrich spring-activated foot and lower leg snares. Snares were set throughout the study area but out of sight of roads and maintained trails. Snares were attached to green drag logs to reduce the incidence of foot injury to captured bears. Snares were checked daily.

Snared bears were immobilized with a combination of ketamine hydrochloride and xylazine hydrochloride (Rompun). The ketamine hydrochloride (100 mg/ml) was freeze-dried and concentrated to 180 mg/ml, then mixed with xylazine hydrochloride (90 mg/ml) in a 2:1 ratio. A 6-foot prod pole was used to administer the drug.

In winter, the denning areas of the bears were located with a radio signal emitted by the bears' collars. Of the 48 bears in the study, 27 were equipped with these collars. In winter, dens had to be entered to immobilize the bears, which were alert.

There were no serious complications from snares, anesthesia, or response to the investigators. After anthropometric measurements were made, a blood sample was removed from the femoral vein. No samples were taken from bears smaller than 28 kg. The sample was cooled; serum was separated from red cells; and urea and creatinine concentrations were determined. Serum urea nitrogen was determined by the diacetyl monoxime colorimetric method (*7*). Serum urea was calculated as

$$\frac{\text{urea nitrogen}}{0.466}$$

Serum creatinine was determined with a creatinine kit (Sigma), which consists of the alkaline picrate colorimetric assay as modified by Heingard and Tiderstrom (*8*). Statistical analysis of changes in blood parameters was done with Scheffe's comparison because seasonal values could not be considered either independent or dependent.

High carbohydrate foods (serviceberry, chokecherry, and acorns) were scarce during the late summer and early fall (15 August to 30 September) of 1981 because of a severe 2-day freeze (−6°C) in late June. In contrast, the berry and acorn crops were moderately abundant in both 1982 and 1983. However, even in the excellent food years, many of the bears that were tracked by radio signals had ceased foraging on soft and hard mast by early October and had left the low-elevation oakbrush.

The pattern of U/C was similar in all 3 years (Fig. 1). In winter, especially by March, the ratio had declined to values of 10 or less. In May and June, none of the samples showed a ratio less than 22. However, in August and September, the U/C had decreased noticeably, 7 of 20 samples showing values of 10 or less and only 5 showing values above 22.

Summer, fall, and winter values of U/C were all significantly different from each other (Scheffe's comparison at a significance level of 0.05) (Fig. 2). For urea, summer values were significantly higher than values for fall and winter. However, fall and winter values were not significantly different from each other. For creatinine, winter values were significantly different from summer and fall values. Thus, the ratio proved to be the best means to show the seasonal differences.

In all 3 years, around the last week of September, the bears left their fall feed-

ing ranges, some moving 10 to 30 km to their previous summer ranges. After these bears had returned to their denning areas, active foraging did not appear to take place. Presumably, these animals had reached or were close to the condition of physiological-biochemical adaptation that permits them to be independent of food and water for months.

Den entry times were similar in all 3 years, with no noticeable difference in timing related to elevation. Median den entry times were the last week of October in 1981 (n = 20), and the first week of November in 1982 (n = 24) and 1983 (n = 21). More than 65 percent of the bears tracked with radio signals denned during the 3-week period having the median week as the center week. Thus, most of the bears were denning 2 to 5 weeks after leaving the fall feeding areas. A few bears did not den until the first week of December, 8 to 9 weeks after leaving their fall feeding areas. Regardless of the home range site, there is very little nutritionally valuable food available after mid-October. Why the bears studied deferred denning until the times observed is unknown, but it appears that they are physiologically ready to do so much earlier.

Since not all bears achieved U/C values of 10 or less in late summer or early fall, but all eventually did so in winter, the adaptation required for successful denning appears to be a slowly developing process. Gradual changes continued to occur in denning bears. For instance, pulse rates reached their lowest levels at the end of December (*2*). Serum thyroxine and triiodothyronine gradually decrease throughout denning (*9*). In the male bear, the testosterone level is lowest in October but gradually increases during hibernation to values approaching those occurring in the mating season (*10*).

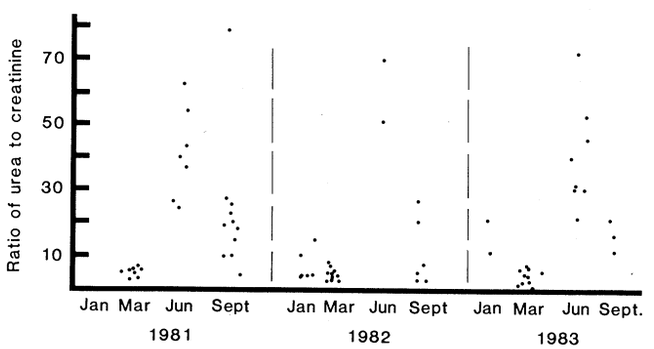

Fig. 1. Ratio of urea to creatinine in sera of wild black bears.

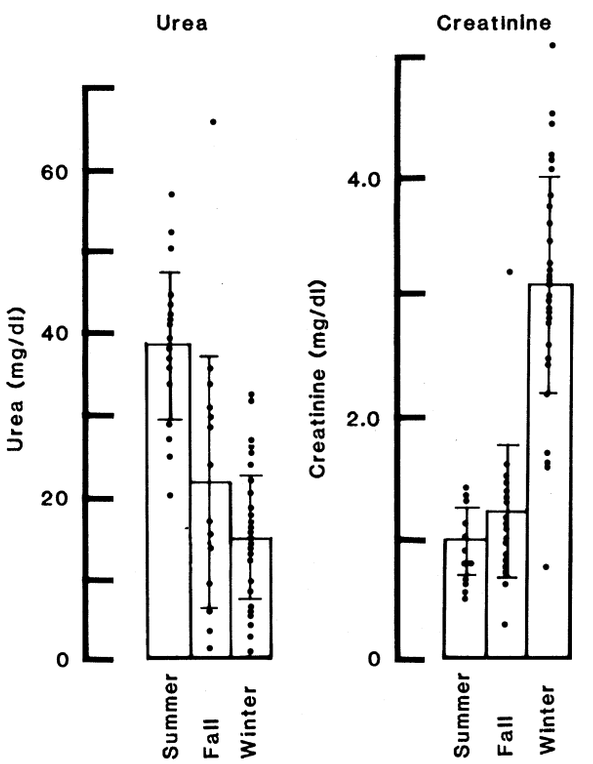

Fig. 2. Seasonal levels (means ± standard deviation) of urea and creatinine in sera of wild black bears. During the 3-year period, the numbers of bears studied in summer, fall, and winter were 16, 20, and 27, respectively.

Other data indicate that the adaptation of hibernation persists into the spring, after the bears have left their dens. For instance, in captivity, despite free access to food and water, a grizzly bear (*Ursus arctos*) studied 3 weeks after it emerged from the den, ate no food and drank little water. Urination occurred in small amounts, varying between 140 to 180 ml/day (*11*). Wild bears also seem to eat little after emerging from their dens. Springtime may represent a gradual lessening of the denning adaptation.

Thus, these circumannual findings show that the "umbrella of hibernation," which permits the bear to be independent of food and water, appears to occur before the bear enters its den and persists after it leaves the den. The bear apparently begins preparation for denning while food is available, and the metabolic adaptations responsible for freedom from the need for food and water persist into spring when food is usually scarce.

A biological indicator of this hibernation adaptation is a U/C ratio of 10 or less, and this is independent of the sex of the bear and whether the female is solitary, pregnant, or lactating.

RALPH A. NELSON
Department of Research, Carle Foundation Hospital, and *College of Medicine, University of Illinois, Urbana 61801*

THOMAS D. I. BECK
Division of Wildlife, Department of Natural Resources, Denver, Colorado 80216

DIANNE L. STEIGER
Department of Research, Carle Foundation Hospital

References and Notes

1. R. A. Nelson, *Fed. Proc. Fed. Am. Soc. Exp. Biol.* **30**, 2955 (1980).
2. G. E. Folk, Jr., *Textbook of Environmental Physiology* (Lea & Febiger, Philadelphia, 1974), pp. 280–309.
3. R. A. Nelson, H. W. Wahner, J. D. Jones, R. D. Ellefson, P. E. Zollman, *Am. J. Physiol.* **224**, 491 (1973).
4. R. A. Nelson, G. E. Folk, Jr., E. W. Pfeiffer, J. J. Craighead, C. J. Jonkel, D. S. Wellik, in *International Conference on Bear Research and Management*, E. C. Meslow, Ed. (International Association for Bear Research and Management, Calgary, 1983), vol. 5, p. 284.
5. R. A. Nelson, D. L. Steiger, T. D. I. Beck, *Acta Zool. Fenn.* **174**, 137 (1983).
6. R. A. Nelson, J. D. Jones, H. W. Wahner, D. B. McGill, C. F. Code, *Mayo Clin. Proc.* **50**, 141 (1975).
7. R. J. Henry, D. C. Cannon, J. M. Winkelman, Eds., *Clinical Chemistry—Principles and Techniques* (Harper & Row, New York, ed. 2, 1974), pp. 514–517.
8. D. Heinegard and G. Tiderstrom, *Clin. Chim. Acta* **43**, 305 (1973).
9. F. Azizi, J. Mannix, D. Howard, R. A. Nelson, *Am. J. Physiol* **237**, E227 (1979).
10. J. M. McMillin, U. S. Seal, L. Rogers, A. W. Erickson, *Biol. Reprod.* **15**, 163 (1976).
11. G. E. Folk, Jr., and R. A. Nelson, *Proceedings of the Fifth International Symposium on Circumpolar Health* **81**, 617 (1981).

24 February 1984; accepted 20 June 1984