Bone nitrogen isotope composition and climate

SIR—Heaton *et al.*[1] report that the $^{15}N/^{14}N$ ratios of bone collagen from prehistoric humans with little or no access to marine protein show a negative correlation with present rainfall levels in the areas of South Africa they inhabited. Such a correlation cannot, however, be accepted uncritically, because the influences of dietary differences among such populations have not been considered. For example, $^{15}N/^{14}N$ ratios of bone collagen of early historic Griqua pastoralists from the arid interior of Orange Free State are higher than those of late prehistoric Iron Age farmers of the Northern Transvaal[2]. This is expected given the well-known trophic level effect on nitrogen isotope ratios of bone collagen[3]. The data for these two populations, if plotted together against rainfall, would produce a regression similar to that obtained by Heaton *et al.*, but would not reflect only climatic influences. Thus the authors' interpretation of the nitrogen isotope ratios for human bone collagen based strictly on climate seems to be premature.

By contrast, their data for modern herbivores demonstrate a correlation between rainfall levels and the nitrogen isotope ratios of bone collagen that cannot be ascribed to dietary differences because no relationship between plant $^{15}N/^{14}N$ ratios and rainfall was observed[1]. The authors suggest that the higher ratios of "mammals in arid areas are therefore more likely to be linked with the nitrogen metabolism in the body of the animal itself". In the absence of more specific explanations we feel compelled to summarize our own model and correct a potential flaw in its original presentation[4].

The enrichment of ^{15}N in the bone collagen of East African water-conserving herbivorous mammals relative to water-dependent ones that we reported suggested a relationship between physiological mechanisms of water conservation and nitrogen isotopic mass balance[4], as follows. Urea, the major form in which nitrogen is excreted by mammals, is known to perform an essential function in urinary water conservation[5]. Herbivorous mammals on diets high in protein have the capacity to excrete a highly concentrated urine under conditions of heat and water stress. This is accompanied in most species by an absolute and sometimes spectacular increase in urea output, as in the dikdik[6] and two cattle breeds[7], though not in the camel[8] or in cattle on low-protein diets[7]. Urine in *Bos taurus* has been shown to be depleted in ^{15}N relative to the diet, with the depletion being greater during the day than at night[9] (when water stress is presumably lower). If this difference occurs in all mammal species, animals under more continuous water stress would respond by excreting a more concentrated urine with a quantitative increase in the excretion of ^{15}N-depleted urea, resulting in higher $^{15}N/^{14}N$ ratios in the unexcreted nitrogen. In order to satisfy mass balance constraints, the tissues synthesized from this remaining nitrogen pool in water-conserving, urea-excreting mammals should have higher $^{15}N/^{14}N$ ratios than those of mammals that do not conserve water and/or intensively recycle urea. Such a mechanism would explain the nearly one-to-one correlation in rank order we have found between maximal urinary osmolality[7] and mean bone collagen $^{15}N/^{14}N$ ratios for zebu cattle, donkey, impala, goat, sheep and dikdik[4], and most of the data for herbivores presented by Heaton *et al*[1].

This model is only a hypothesis but it can be tested by controlled water-stress experiments and analysis of nitrogen isotopic mass balance in animals living in different climates and microhabitats. Until the contributions of ecological and physiological processes to variation in animal tissue nitrogen isotope ratios are more clearly understood, palaeodietary analysis based on $^{15}N/^{14}N$ ratios of bone collagen must be regarded as uncertain in all but the simplest of ecological contexts.

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Signal-transduction

SIR—Wakelam *et al*[1], as discussed in News and Views by Petersen and Bear[2], have demonstrated that although concentrations of glucagon above 10^{-8} stimulate the intracellular concentration of cAMP but not of inositol phosphates in hepatocytes, low concentrations (10^{-9}M) increase inositol phosphates but not cAMP. We would like to draw attention to the corresponding effects of ACTH on cells from the rat whole adrenal cortex; concentrations of ACTH above 10^{-10} M stimulate cAMP levels but neither ^{32}P incorporation into phosphatidic acid and phosphatidylinositol nor the production of inositol phosphates, whereas ~ 10^{-12} M ACTH produces the opposite results[3,4]. Moreover, we have obtained similar results using rat zona fasciculata–reticularis (ZF–ZR) adrenocortical cells[5,6] and have shown that high concentrations of ACTH inhibit the increase in production of inositol phosphates by angiotensin II in ZF–ZR cells[7].

Wakelam *et al.*[1] also report that TH-glucagon, an agonist for all the biological effects of glucagon, is effective in stimulating the production of inositol phosphates but not the intracellular concentrations of cAMP. There are also ACTH analogues that are effective in stimulating steroidogenesis in ZF–ZR cells but are only weakly active in activating adenyl cyclase[8]. Their activity in stimulating phospholipase C would now be of interest.

The steroid output of ZF–ZR cells is stimulated mainly by ACTH-like peptides but zona glomerulosa (ZG) cells of the adrenal cortex, which produce aldosterone, are stimulated by many different factors. These factors employ either the adenyl cyclase or phospholipase C system[6]. There are as yet no reports of ZG stimulators acting through both systems in the concentration-dependent manner of ACTH in ZF–ZR cells. This would be an appropriate area for further study.

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Achieved spacetime infinity

SIR—In his review[1] of my book with John Barrow, *The Anthropic Cosmological Principle*, Press accuses us of indulging in "a distressing amount of mathematical flim-flan . . . For example, . . . Barrow and Tipler [claim] 'A Penrose diagram allows us to define rigorously "an achieved infinity", a concept whose logical consistency philosphers have been doubtful about for thousands of years'. This is a silly assertion, but it is put forth with the utmost gravity, in such a way that many readers will be taken in. And it is only one of many such cases." I cannot comment on the "many such cases" which