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Adipose Tissue in Human Infancy and Childhood: An Evolutionary Perspective

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ABSTRACT Humans diverge from most mammals, including nonhuman primates, by depositing significant quantities of body fat in utero and are consequently one of the fattest species on record at birth. While explanations for the fat layer of human neonates have commonly assumed that it serves as insulation to compensate for hairlessness, empirical support for this hypothesis is presently weak. Whether the tissue's abundance at birth and growth changes in adiposity during infancy and childhood might be explained in light of its role as energy buffer has not been assessed, and this possibility is explored through development of a model of fat function and growth centered on two related hypotheses. The first is that the greater adiposity of human neonates is at least partially explainable as an accompaniment of the enlarged human brain, which demands a larger energy reserve to ensure that its obligatory needs are met when the flow of resources from mother or other caretakers is disrupted. The second is that age-related changes in the likelihood of experiencing such disruption have influenced the pattern of investment in the tissue, reflected today in peak adiposity during infancy and a decline to a leaner childhood period. Nutritional disruption is common at birth and until lactation is established, during which time human newborns survive from fats deposited prenatally, suggesting one possible explanation for the early onset of fat deposition. At weaning, the transition from breast milk to supplemental foods and the parallel transition from maternal to endogenous immune protection interact to increase the frequency and impact of nutritional disruption, and this may help explain why newborns devote roughly 70% of growth expenditure to fat deposition during the early postnatal months. Evidence is presented that fat stores are mobilized during infections, hinting at one possible mechanism underlying the association between nutritional status and infectious morbidity and mortality among infants in nutritionally stressed human populations. Consistent with the proposed hypothesis, well-fed infants acquire peak fat reserves by an age of peak prevalence of malnutrition, infectious disease, and fat reserve depletion in less-buffered contexts, and childhood—characterized by minimal investment in the tissue—is a stage of reduced risk of energy stress. The model presented here foregrounds energy storage in adipose tissue as an important life-history strategy and a means to modify mortality risk during the nutritionally turbulent period of infancy. Yrbk Phys Anthropol 41:177–209, 1998.

TABLE OF CONTENTS

Modern humans have been described as an "obese" species, and this characteristic is most apparent in the abundant "baby fat" present at birth (Widdowson, 1950; Pond, 1997). Although it is popular wisdom that a chubby baby is a healthy baby, the fat percentage of the human newborn is exceptional by mammalian standards, exceeding that of even the pinneped seals (Oftedal et al., 1989). Studies of domesticated and wild species reveal that most mammals, including nonhuman primates (Schultz, 1969; Lewis et al., 1983), do not begin to deposit white fat until after birth (Adolph and Heggeness, 1971). The precocious condition of adipose tissue development at birth, despite the human newborn's otherwise altricial state (Watts, 1990), highlights the timing of fat deposition as an atypical feature of human somatic development and raises questions about the evolutionary origins and function of this developmental shift. Moreover, if a chubby baby is indeed a healthy baby, it remains to be explained why this is not necessarily true for other mammals, including our closest kin.

The plumpness of the human newborn has long been recognized as a trait in need of explanation among growth researchers. In his study of US children, Garn (1956:246) noted that human neonates are fatter than other mammals at birth and described early infant fat deposition as a puzzling diversion of resources during a critical stage of development: "There remains, of course, the problem of why the subcutaneous fat behaves as it does during early infancy, and this problem includes both the rapid accumulation of fat at a time when energy requirements for growth are at their maximum, and the seem-

ing failure of the stored fat to contribute to the general motion of growth." In passing, he offers that the fatness of human infants is likely "an evolutionary adaptation to the thermoregulatory problems faced by the young of a glabrous [hairless] wide-ranging homeotherm" (Garn, 1956:232). This assertion was by no means unique (Thomas, 1911), and today the most common explanation for the ample fat layer of the human neonate assumes that it arose as insulation to compensate for the distinctive human lack of the normal mammalian fur coat (Hardy, 1960; Morgan, 1982; Sinclair, 1985; Harsha, 1986; Lowrey, 1986; Prechtl, 1986). For instance, Pretchl (1986:348) notes the paucity of fat in the newborn monkey and suggests that the abundance of this tissue at birth in the human "may be an adaptive compensation for the loss of a fur." In his human growth text, Sinclair (1985:52) similarly suggests, "Fat [is plentiful] in the new-born baby, probably as an insulation against cooling."

The few evolutionary hypotheses that attempt to explain the ponderous condition of humans generally and human infants in particular similarly assume a connection between the loss of fur during hominid evolution and a parallel need for compensatory insulation from subcutaneous fat stores. It was the ample adipose layer of humans and its apparent similarities to that of seals and whales that prompted Alistair Hardy to consider the possibility of an aquatic origin for modern humans, a perspective now known as the "aquatic ape" hypothesis (Hardy, 1960). The abundance and anatomical features of human adipose tissue, especially at birth and during infancy, have been central to Elaine Morgan's (1982, 1994) recent embellishments to Hardy's hypothesis, as outlined in several popular books devoted to the topic. Notable among the tissue's characteristics that she explores is its subcutaneous distribution, which she emphasizes is rare among terrestrial mammals and potentially well suited to conserve heat. In *The Naked Ape*, Desmond Morris (1967:48) reviewed Hardy's hypothesis with interest but finally rejected its aquatic elements, proposing his own scenario to account for both hairlessness and adiposity as coupled features of a uniquely human thermoregulatory solution to a hunting lifestyle on the savanna: "It is interesting that the [loss of hair] was accompanied by the development of a sub-cutaneous fat layer, which indicates that there was a need to keep the body warm at other times....The combination of reduced hair, increased sweat glands, and the fatty layer under the skin appears to have given our hard-working ancestors just what they needed, bearing in mind that hunting was one of the most important aspects of their new way of life."

Despite the tissue's assumed importance as insulation, evidence for this function in humans and in terrestrial mammals more generally is equivocal (Eveleth and Tanner, 1976; Pond, 1978). Pond (1991, 1997) has reviewed the literature on body-fat insulation in vertebrates, including humans, and concludes, "The insulation theory is widely quoted in both the learned and the elementary biological literatures, almost invariably without supporting anatomical or experimental evidence....In spite of its widespread acceptance, very few data support the insulation theory, even in the case of some aquatic mammals" (Pond, 1991:205). Most but not all research among circumpolar human populations reports comparable or even thinner subcutaneous fat stores compared to temperate-latitude peers, suggesting that the tissue's properties as insulation may play only a minor role in human adaptation to cold, at least among children and adults (Eveleth and Tanner, 1976; Stini, 1981), and there is surprisingly little evidence that fat stores influence body temperature in human newborns (Johnston et al., 1985).

It is widely accepted that the primary function of mammalian body fat is to serve as energy store (Pond, 1978; Cahill, 1982; Norgan, 1997), and developmental changes in adiposity during other stages of the human life cycle are understood as preparation for future energetic challenges, a notable example being the rapid fat deposition of females at puberty and the subsequent contribution of this tissue to the energetics of pregnancy and lactation (Stini, 1981; McFarland, 1997). The rate of deposition and level of adiposity during infancy are comparable or even greater, in relative terms, to that of

the adolescent female, and there is reason to question whether the abundance and pattern of fat growth during early life might also reflect the tissue's role as energy buffer. For one, recent evolutionary perspectives on hominid encephalization hypothesize that the metabolic needs of the enlarged human brain required a suite of dietary adaptations to sustain its energy requirements (Foley and Lee, 1991; Leonard and Robertson, 1992; Aiello and Wheeler, 1995; Bogin, 1997), and by implication the human infant—whose brain devours fully half of total metabolic expenditure—may face energetic challenges unique among mammals. Second, energy deficiency associated with malnutrition and infectious disease is recognized as a primary contributor to human infant mortality (Waterlow and Payne, 1975; Pelletier et al., 1993), which could heighten selection for energy storage during infancy. The early growth trajectory of adipose tissue—which contributes to a rapid rise to peak adiposity during infancy followed by a subsequent decline to a lean childhood (Fomon et al., 1982)—has been explained only insofar as it relates to developmental changes in proximate determinants of energy balance, such as physical activity and appetite (e.g., Holliday, 1986). What is less clear is how these developmental changes in expenditure and intake are coordinated to produce the observed pattern of investment in the tissue (Garn, 1956) and whether the ensuing growth trajectory reflects the function of the tissue in early development, akin to the more widely appreciated match between fat form and function in adolescent females.

Thus, important questions remain about this costly feature of early human ontogeny. First, why do humans give birth to the fattest newborns on record? Second, are the developmental changes in adiposity and body composition that are prominent features of early human ontogeny functional? In an attempt to shed light on these and related questions, this article first reviews available data on neonatal mammalian body composition to provide a baseline for consideration of the adiposity of human newborns. Discussion then focuses on the energetic challenges faced by human infants—such as large brain size, parturition, the weaning transition, and infectious disease burden—which are hypothesized to help explain the greater fatness of human newborns relative to those of other mammals and developmental changes in the metabolic drive to deposit fat during early human development. Evidence for the tissue's insulative function in humans is briefly considered, but the reader interested in more comprehensive coverage of this material is referred to recent reviews by Shephard (1991), Frisancho (1993), and Pond (1997).

Although evolutionary theory is not prominent in this review, the approach is inspired by life-history theory, which seeks to explain the evolution of the major features of life cycles, including such factors as the distribution of age-specific death and fertility rates, growth rates, age at maturity, and the number and size of offspring (for a review see Stearns, 1992). Demography lies at the heart of life-history theory, as life histories are viewed as evolving in response to changing environments via effects on age-specific mortality and fertility rates (Partridge and Harvey, 1988). Among the theory's central assumptions is the allocation rule, which recognizes that organisms must allocate finite time and energy to a range of competing functions, such as growth, maintenance, reproduction, or energy storage (Stearns, 1992; Hill, 1993). Following in part from this problem of managing finite resources, life histories are viewed as balancing trade-offs between competing functions in a fashion that approaches an optimal strategy for the species (Charnov, 1993; Hill, 1993). In the spirit of this approach, the second section of this article explores age changes in nutrition-related morbidity and mortality rates for insights into the possible adaptive basis of the pattern of fat growth in human infants and children, which is balanced by considerations of a range of alternative nonadaptive explanations at the end of the review (Williams, 1966; Gould and Lewontin, 1979).

BODY COMPOSITION AT BIRTH IN MAMMALS

To provide a mammalian frame of reference for human neonatal adiposity, published data on body composition at birth are compiled in Table 1 and plotted in Figure 1.

TABLE 1. Percentage fat at birth and birth weight in mammals

Species	% fat at birth	Birth weight (g)	Source
Human	15	3,000	Widdowson, 1950
Guinea pig	10.8	80	Raffel et al., 1996
Harp seal	10.4	10,800	Worthy and Levigne, 1983
Fur seal	6	4,000	Arnoud et al., 1996
Sea lions	4.8	8,300	Oftedal et al., 1987
Reindeer	4.4	4,400	Ringberg et al., 1981
Baboon	3	950	Lewis et al., 1983
Lamb	3	—	McCance and Widdowson, 1977
Calf	2.8	—	McCance and Widdowson, 1977
Foal	2.6	—	McCance and Widdowson, 1977
Black bear	2.3	394	Oftedal et al., 1993
Mouse	2.1	2	Widdowson, 1950
Elephant seal	2	39,000	Bryden, 1969
Rabbit	2	54	Widdowson, 1950
Cat	1.8	118	Widdowson, 1950
Caribou	1.8	5,650	Gerhart et al., 1996
Pig	1.3	84	Manners and McCree, 1963
Rat	1.1	6	Widdowson, 1950
Hamster	1	—	Adolph and Heggeness, 1971

Studies of common domesticates such as rats, pigs, and sheep and wild species such as black bear reveal that these species do not begin to deposit significant fat stores until the onset of suckling and are thus born lean, with roughly 1–4% of body weight as fat (Spray and Widdowson, 1950; Adolph and Heggeness, 1971). The fat content of the newborn baboon has been estimated at 3% (Lewis et al., 1983), and Schultz (1969:23) has described newborn captive great apes as "decidedly 'skinny' and horribly wrinkled" due to their lack of subcutaneous adipose tissue. Although neonatal body composition data from a range of primate taxa will be necessary to establish this more definitively, these observations suggest that primates may not diverge from the common mammalian pattern of a postnatal onset of fat deposition. Humans clearly do, however, as they begin to deposit fat during the third trimester of pregnancy and rapidly attain a fat mass that represents roughly 15% of body weight at term (Spray and Widdowson, 1950; Fomon, 1966). Thus, despite being the most altricial of primates at birth in terms of skeletal maturation (Watts, 1990), humans appear to have a head start on most mammals, including primates, with respect to fat deposition.

Scaling relationships

Many biological features of organisms—such as metabolic rates, growth rates, and birth weights—vary systematically as a function of body size, and allometric analyses are commonly used to assess trait variation with the effects of body size removed (see Harvey and Pagel, 1991). Pond and Ramsay (1992) have previously shown that fat mass in specific depots scales to body size in adult mammals, and I have extended a similar analysis to mammalian neonates in Figure 2 using data from Table 1. The limitations of this analysis must be emphasized, as the data on neonatal body composition are sparse, with nonhuman primates especially poorly represented. The small sample size has precluded assessment of the most appropriate taxanomic level of analysis, and thus the present investigation proceeds under the problematic assumption that each species represents an independent data point (Harvey and Pagel, 1991). In light of these limitations, the following results should be viewed as preliminary and, one hopes, as stimulus for further data collection and more rigorous assessments.

The best-fitting equation reveals that fat mass at birth scales to birth weight with an exponent of 1.12, suggesting that larger-bodied species tend, on average, to have a slightly greater percentage fat mass at birth. The 450 g of fat present at birth in the 3,000 g human (Widdowson, 1950) is roughly 3.75 times greater than the 122 g of fat expected for a mammal of human size, which is a statistically significant diversion from the

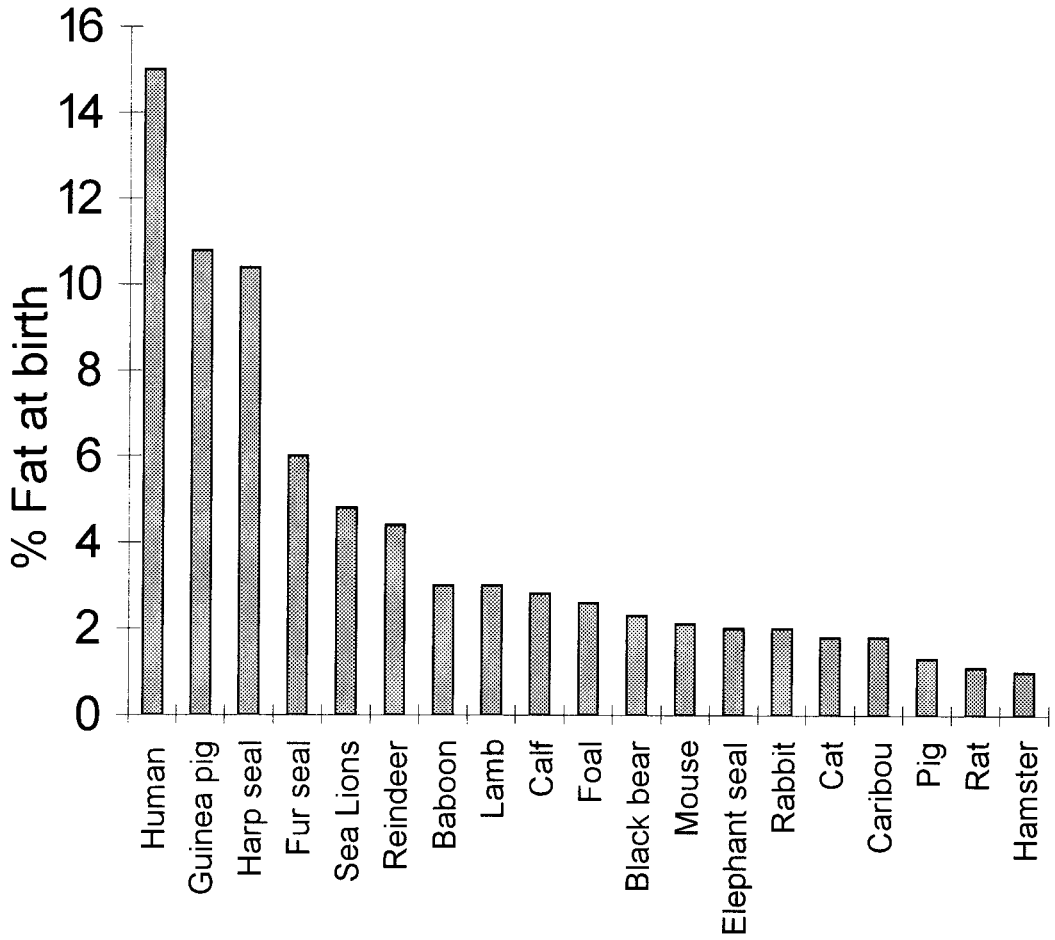

Fig. 1. Percentage fat at birth in mammals (see Table 1 for references).

best-fitting trend (95% C.I. = 36.8–400.7 g). The two other species with greater fat mass than predicted for their birth weight—guinea pigs (4.2 times expected fat mass, $P < .05$) and harp seals (2.2 times expected fat mass, $P > .05$)—are highlighted, as explanations for their prenatal fat deposition are considered later in the review.

What requires explanation in humans? Brown vs. white fat

Available data on neonatal body composition are thus consistent with the common view that humans are fatter than other mammals at birth (Garn, 1956; Schulz, 1969; Pond, 1978; Tanner, 1990). However, adipose tissue comes in two physiologically and functionally distinct forms in the newborn—brown fat and white fat—and examination of the relative abundance of each reveals more precisely how human neonatal adiposity differs from that of most mammals. Newborn mammals are unable to raise body temperature through shivering but instead are endowed with specialized depots of brown adipose tissue (BAT), which is distinct from white adipose tissue (WAT) by virtue of a rich supply of blood vessels and heat-producing mitochondria (Aherne and Hull, 1966; Symonds and Lomax, 1992). Brown fat cells generate heat by uncoupling the electron gradient in oxidative phosphorylation, a process stimulated by the sympathetic nervous system and thyroid hormones

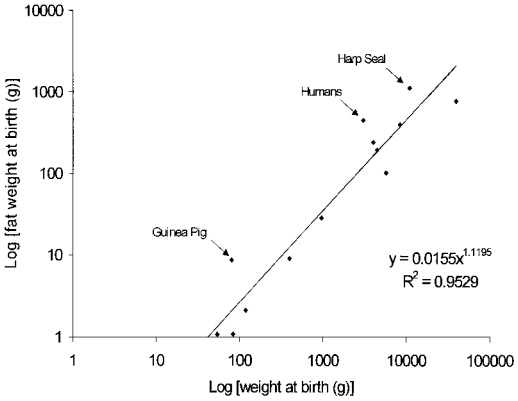

Fig. 2. To remove the effects of body size, the scaling relationship between fat mass and birth weight is assessed using mammalian body composition and birth weight data from Table 1. Based upon the best-fitting equation, fat mass scales to birth mass with an exponent of 1.12, revealing that the proportion of birth weight represented by fat increases with increasing size. Humans deposit roughly 3.75 times the fat mass predicted for a neonate of their size at birth, which is a statistically significant divergence from the best-fitting trend (see text for discussion). Guinea pigs and harp seals are born with fat levels near that of humans, and the depositional patterns of these species relate to energy stress experienced during the early postnatal period.

and fueled by triglycerides stored within the tissue (Williamson, 1986; Arbuthnott, 1989). The role of BAT in infant thermoregulation is demonstrated by thermographic images revealing heightened body surface temperature over BAT depots (Rylander et al., 1972), and by studies linking the hypothermia of malnourished infants to lipid depletion in BAT deposits (Brooke et al., 1973). However, while important, this tissue is not especially abundant in humans. Cold-climate species such as musk ox, caribou, reindeer, walrus, and various species of seal are born with massive BAT depots and higher metabolic expenditure but little if any subcutaneous WAT (Blix and Steen, 1979; Blix et al., 1984). This pattern is opposite to that of the newborn human, who is born with massive WAT stores but an abundance of BAT (1–3% of birth weight) typical of most mammals (Aherne and Hull, 1966; Pretchl, 1986). Thus, what requires explanation in humans is the remaining 12–14% of birth weight represented by white fat, which is excessive relative to any mammal for which data is available and accounts for the divergence of human neonates from the allometric trend discussed above.

ADIPOSE TISSUE AS INSULATION

Insulation from white fat deposited in subcutaneous depots is one tactic available to homeotherms to reduce the rate of heat loss (Blix and Steen, 1979), and, as noted, this is the most common explanation for the abundant fat layer of human newborns (e.g., Garn, 1956; Sinclair, 1985; Lowrey, 1986; Behrman et al., 1992). Although human neonates are good candidates for an insulatory layer due to their large surface area per kilogram of body weight and consequent high rate of heat loss (Alexander, 1975), fat deposition in subcutaneous depots is generally not enhanced in human adaptation to cold stress, and evidence for this function in infants and newborns is similarly weak. Some studies of Eskimo and other circumpolar populations reporting anthropometric data for adults, children, and—less frequently—infants have documented comparable or even thinner skinfold thickness compared to reference data from lower latitude populations (Schaefer, 1977; Eveleth and Tanner, 1976; Johnston et al., 1982; Shephard, 1991). The common finding of increased metabolically active lean mass in such groups—in combination with average or reduced skinfold thickness—has been interpreted by some as evidence that the capacity to generate heat rather than to conserve it is of primary importance in human adaptation to cold (e.g., Stini, 1981; Johnston et al., 1982). In his review on evolution and human body composition, Stini (1981:58) observed, "Humans are among the fattest of mammals, but do not adapt to cold climates to any significant degree through the acquisition of thick layers of subcutaneous fat." Eveleth and Tanner (1976:269) review International Biological Programme investigations of circumpolar populations and similarly conclude, "Apparently a thick layer of subcutaneous fat is not the biological adaptation made in the Arctic by indigenous inhabitants."

In cases where thicker skinfolds are reported in such populations, interpretations vary. Beall and Goldstein (1992) documented a higher trunk-to-extremity skin-

fold ratio among children and female Moost nomads from Mongolia, which they interpret as an adaptation to reduce heat loss and possibly a means to increase the mass of thermogenic fat. Although infants were not included in this sample, Leonard and coworkers (1994) report similar fat patterning in children and females of the Evenki reindeer herders of Siberia and thicker skinfolds among infants in this group compared to US reference data; they propose that the pattern of fat deposition in this population may be an adaptation to conserve heat. Haas et al. (1982) reported thicker skinfolds among infants from a highland Andean group compared to lowland peers, but they cite a lack of evidence for an adaptive increase in subcutaneous fat among infants in cold environments and suggest that differences in body surface area, diet, or differential effects of high altitude hypoxia on length and weight growth could explain the thicker skinfolds of the highland group.

Studies designed to identify the determinants of infant and neonatal body temperature have generally shown that metabolically active tissues—such as BAT stores and muscle mass—are critical to thermoregulation but provide only limited evidence for an insulative role for subcutaneous fat. Brooke (1973) has shown that marasmic children with severely depleted fat and muscle have lower total specific insulation relative to infants with kwashiorkor, whose fat stores are often better maintained and even augmented in some cases by water retention and edemia. However, correlations between thermal insulation and rectal temperature in these infants were only significant at night, and in a separate study of similar malnourished infants the author concluded that "the main thermoregulatory failure in these children was that they did not increase their heat production in response to cold stress" (Brooke et al., 1973:86), a fact possibly explained by their nutritional state and depleted brown fat deposits and further supported by the finding that such infants regain a normal body temperature within several hours of feeding (Brooke, 1972). One of the only studies to explicitly assess the importance of subcutaneous fat to thermoregulation in newborns found that measures of lean body mass were significant predictors of body temperature and temperature stability, while neither thermal variable related significantly to either triceps or subscapular skinfold thickness (Johnston et al., 1985). The authors concluded, "The thickness of the subcutaneous layer of fat in newborns does not seem to contribute to the body temperature or to its consistency in the first few days following birth" (Johnston et al., 1985:345).

These findings do not deny the fact that fat insulates when deposited subcutaneously, as surely it must (Shephard, 1991). The finding of thicker infant skinfolds in at least one circumpolar population (Leonard et al., 1994) may hint at a greater insulative role for the tissue among infants in cold-adapted populations, and whether fat located in intraabdominal depots conserves heat in infants by contributing to body mass and heat-conserving body contours, as suggested for Moost children and adults (Beall and Goldstein, 1992), warrants consideration. Further anthropometric data on skinfold thickness related to metabolic expenditure or temperature stability in a range of thermal environments are needed to clarify the importance of white fat as a factor in human neonatal and infant thermoregulation. However, at present the common assumption that the abundance of this tissue in human neonates evolved to insulate is best viewed as a hypothesis awaiting empirical verification.

ADIPOSE TISSUE AS ENERGY STORE

What is more certain is that the tissue's role as energy store has precedence when the body is faced with energy stress, at least in humans (for reviews see Young and Scrimshaw, 1971; Cahill, 1982). At the onset of a fast, hepatic glycogen stores are rapidly depleted, and the body's normal reliance upon glucose is initially sustained through hepatic gluconeogenesis (glucose production) fueled by amino acids released from muscle protein. The principal metabolic adaptation during starvation involves a shift away from gluconeogenesis and carbohydrate metabolism to a primary reliance upon lipids stored in adipose tissue to sustain metabolism. Glucagon, cortisol, and other

catabolic hormones are elevated during a fast and stimulate breakdown of adipose tissue triglycerides (lipolysis) to free fatty acids (FFAs) and glycerol, the latter entering the liver as a gluconeogenic precursor. Free fatty acids enter directly into oxidative metabolism in tissues such as skeletal muscle and the heart but must be converted in the liver to the ketone bodies acetoacetate and β-hydroxydbutyrate for use in obligate glucose-using organs, such as the tissues of the central nervous system.

The body's capacity to use FFAs, glycerol, and ketone bodies to sustain metabolic needs spares lean tissue, and this is recognized as increasing the duration of survivable fast (Cahill, 1982). However, some species known to rely upon subcutaneous fat stores for insulation, such as gray and elephant seals, protect subcutaneous depots after prolonged starvation by increasing mobilization and use of amino acids from lean tissue, suggesting that the distribution of body fat per se is an adaptation to conserve heat in such species (Oritsland et al., 1985; Castellini and Costa, 1990). In human infants, the proportion of body fat located in subcutaneous depots is reduced during malnutrition (Stini, 1981), demonstrating that depots likely most critical for conserving body heat are the first to be mobilized when energetic reserves are required. This suggests but certainly does not prove that the tissue's property as an insulative layer is not a primary explanation for the evolution of its abundance in human neonates (e.g., Pond, 1978, 1997). Although the importance of stored fats as an energy reserve is implicit in the use of skinfolds as measures of nutritional status during infancy and childhood (Frisancho, 1974; Martorell et al., 1976), whether human neonatal adiposity might be explained in light of its role as an energy buffer has not been assessed.

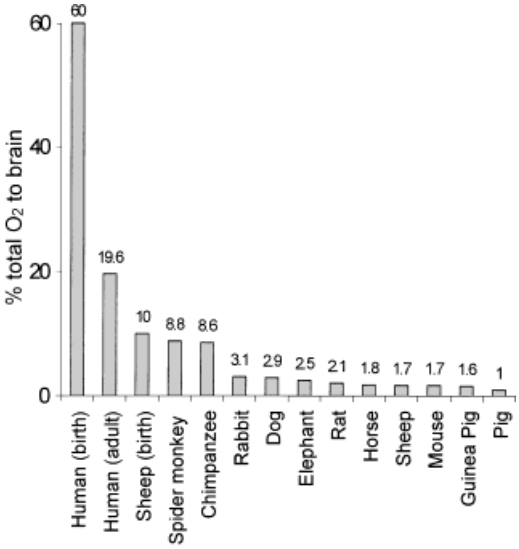

Fig. 3. Cerebral O_2 uptake as a percentage of total body metabolism in mammals. Humans have the largest brain size relative to body size on record and consequently devote a large proportion of total metabolism to meeting the brain's energy needs. It is hypothesized that the greater energy needs of the human brain—which must be supplied from tissue stores during nutritional disruption—may help explain why human infants invest extensively in body fat stores, including the atypical prenatal investment in the tissue (see Table 3 for data and sources).

Evolutionary perspectives on the energetics of human encephalization

Any consideration of the energetics of human infancy is well-served to begin with a discussion of the brain, as the infant's massive brain is estimated to consume 50–60% of total metabolic expenditure (Holliday, 1986). Brain size is one trait—in addition to the lack of an insulating fur coat—that sets human neonates apart from most mammals and thus might help explain features of human neonatal and infant adipose tissue (Fig. 3; Table 2). Interest was perked in the energetics of mammalian brain size by Martin's (1981) observation that neonatal brain size scales to maternal body size with the same exponent as basal metabolic rate (BMR). Martin interpreted this isometric relationship between brain size and BMR (i.e., they are directly proportional) as evidence that maternal metabolic turnover is a limiting factor in encephalization, as brain growth requires energy that must be supplied by the mother's body and metabolism during gestation and lactation (Martin, 1981, 1996). Although focusing on adult mammals, Armstrong (1983:1302) attempts to explain brain/body scaling by reference to the costs associated with meeting the brain's energy metabolism rather than growth and has proposed that "the size of the brain will

TABLE 2. Rates of cerebral oxygen consumption as percentage of total BMR in mammals[1]

Species	Body weight (kg)	Total O_2 (ml/min)	Brain O_2 (ml/min)	Brain %
Human—newborn[2]	3.5	20	12	60
Human—adult	70	250	49	19.6
Sheep—term fetus[2]	3.5	21	2.1	10
Spider monkey	3.8	36	3.2	8.8
Chimpanzee	38	158	13.5	8.6
Rabbit	2.6	21.7	0.7	3.1
Dog	16.4	83.4	2.4	2.9
Elephant	6,650	7,800	200	2.5
Rat	0.25	3.4	0.07	2.1
Horse	600	1,296	23	1.8
Sheep	52	215	3.7	1.7
Mouse	0.027	0.75	0.013	1.7
Guinea pig	0.8	10.3	0.16	1.6
Pig	125	400	4.2	1

[1] Data from Grande (1980).
[2] Data on cerebral O_2 uptake in 3.5 kg sheep fetus and human newborn from Jones (1979).

be constrained both by the size of the system delivering oxygen and glucose and by the rate at which energy can be expended in supporting the brain's constantly high metabolic demands." Her allometric analyses show that primates—including humans—have higher cerebral metabolic expenditure than predicted for mammals of their body size yet have a BMR appropriate for their size, leading her to suggest that "a major primate adaptation appears to have been the allocation of a larger proportion of the body's energy supply for the brain" (Armstrong, 1983:1304).

Anthropologists have focused more specifically on the energetics of hominid encephalization, and the evolutionary models proposed have emphasized that the large brain size of humans—and infants and children in particular—required nutritional or cultural adaptations to compensate for larger cerebral metabolic expenditure. Foley and Lee (1991) estimate that human infants have higher caloric needs than a chimpanzee of comparable body size owing to differences in brain size and hypothesize that encephalization required changes in foraging strategy and dietary quality to provide for the increasing cerebral energy needs of human offspring. They further suggest that encephalization required a slower and less costly rate of growth and a correspondent protraction of development to offset greater cerebral expenditure. Leonard and Robertson (1992, 1994) show that cerebral metabolism scales to resting metabolic rate in anthropoid primates and estimate that humans allocate 3.5 times the percentage of total metabolism to the brain than that predicted for an anthropoid of human body size. Humans also spend more time foraging and consume a higher quality diet than expected for their size, which they hypothesize is explainable in light of their greater cerebral needs. Like Foley and Lee, they single out infancy and childhood as a life stage when the energetic challenge imposed by brain size is particularly acute and propose that a slower growth rate may have been necessary to compensate for greater cerebral expenditure: "A human child under the age of 5 years uses 40–85% of resting metabolism to maintain his/her brain. Therefore, the consequences of even a small caloric debt in a child are enormous given the ratio of energy distribution between brain and body. Hence, the prolonged period of growth in humans may be partly an adaptation to limit the already high total and brain energy requirements during childhood" (Leonard and Robertson, 1992:191). Most recently, Bogin (1997:77) has outlined a hypothesis to explain the extended growth period of humans and similarly views brain size as one feature unique to recent hominids that may have required slowed growth rates but also "a special diet that must be procured, prepared, and provided by older individuals."

Hypothesis 1: Large brain requires larger energy backup. If the underlying premise of these hypotheses is correct, hominid encephalization required the parallel development of specialized nutritional adaptations, reflected in the fact that modern humans—and infants in particular—are reliant upon a constant flow of calorically dense foods to sustain their metabolic needs (Leonard and Robertson, 1992). The greater energy requirements of the encephalized infant may have required enhanced maternal investment or behavioral adaptations to distribute this nutritional burden across relatives (Foley and Lee, 1991; Bogin, 1997). One inference that may be drawn from these analyses is that the supply of energy from body nutrient stores must be proportion-

ately increased in human offspring relative to those of smaller-brained species when the flow of nutritional resources from the mother or other caretakers is impaired, and this may shed light on the greater adiposity of humans neonates.

Possible mechanisms linking brain size and adiposity.

Energetic scenarios. This hypothesis requires justification in light of the finding that human adults have *total* metabolic requirements as predicted for their body size despite having the largest relative brain size of any adult mammal on record (Martin, 1981; Armstrong, 1983). It is presently unclear whether human infants also have total body metabolic rates appropriate for a mammal of their size. Foley and Lee (1991) estimate that the energy needs of a human infant of 12–18 months of age are roughly 17% greater than a chimpanzee of similar body size owing to differences in brain size, and, if correct, this implies that human infants require a larger energy reserve than a chimpanzee infant to survive a fast of comparable duration. However, this estimate was based upon differences in brain size alone, and it is possible that the size of other metabolically active tissues, such as the gut, are reduced in human infants sufficient to at least partially offset their larger cerebral requirements, as has been proposed for human adults (Armstrong, 1983; Aiello and Wheeler, 1995). Whether such repartitioning occurs during infancy has not been assessed but is unlikely to fully compensate energetically for brain size given that the brain requires half of total metabolism at this age, compared to only 20% during adulthood (Holliday, 1986). Further data on BMR and organ size in human and nonhuman neonates and infants are needed to clarify the degree to which reductions in other organs compensate energetically for larger brain size in human infants and more generally whether human neonates and infants have metabolic rates greater than expected for a mammal of their body size.

Even if reductions in other expenditures partially compensate for the infant's larger cerebral needs, having a large brain is still likely to require a larger energy backup during prolonged fasting conditions. By allocating less to functions such as growth or (possibly) gut metabolism (Foley and Lee, 1991; Aiello and Wheeler, 1995) and a large proportion of metabolic output to the brain, most of the human infant's metabolic expenditure is devoted to a function with obligatory and inflexible requirements (McIlwain, 1966; Armstrong, 1983). The capacity to reduce energy expenditure during a fast by slowing or ceasing growth is attenuated for taxa that already devote a small fraction of total expenditure to this function, such as primates (Charnov, 1993), and, as noted, evolutionary trade-offs between growth rates and cerebral metabolism have been hypothesized for human infants (Foley and Lee, 1991; Leonard and Robertson, 1992; Bogin, 1997). Reductions in the size and expenditure of metabolically active tissues and organs reduce the metabolic rate during prolonged starvation in many species (Oftedal et al., 1989), and this capacity may also be blunted if expenditure on such systems is reduced to free energy for a larger brain. The importance of this mode of adaptation has been documented in human adults, as evidenced by the observation that the mass of some metabolically costly tissues, such as the organs of the gastrointestinal tract, may be reduced by 50% during starvation (reviewed in Keys et al., 1950). In contrast, cerebral metabolism is considered stable (McIlwain, 1966), and mass reductions in the brain greater than 5% are rarely observed, even after prolonged starvation (Keys et al., 1950). Thus, even if the energy needs of the large human brain in the resting state are offset by reductions in the size or expenditure of other metabolically costly tissues or through reduced growth rates during the growing years, diverting energy away from these flexible expenditures to the brain—which has a comparably stable mass and metabolic rate during a fast—is likely to require a larger energy backup as compensation. This perspective predicts that the capacity to reduce metabolic rate facultatively will be impaired in humans relative to other comparably sized but smaller-brained species.

TABLE 3. Substrate deposition in the growing human brain, birth to 12 months[1]

Age	Brain weight (g)	% lipid	% protein	% water	Lipid (g)	Protein (g)	Water (g)
Birth	447	2.6	6.2	89.6	11.6	27.7	400.5
12 months	920	6.1	8.2	83.9	56.1	75.4	771.9
Gain (B–12)	473	9.4	10.1	78.5	44.5	47.7	371.4

[1] Data on brain weight, male/female average, from Schulz et al. (1961). Data on human brain composition from White et al. (1991). Brain composition at 18 months used as estimate of composition at 12 months.

Brain growth is not costly. In addition to its formidable rate of energy consumption, the brain grows rapidly in utero and, in humans, during the first two years of postnatal life (Dobbing and Sands, 1973). It has been suggested that brain growth per se carries significant nutritional costs for infant and mother (Martin, 1981, 1996; Bogin, 1997), and, if so, it might follow that humans require larger adipose depots as a backup substrate supply for brain growth and myelination during periods of nutritional disruption. Data on the mass and chemical composition of the human brain are available for the first year of life, allowing calculation of substrate deposition in the growing brain during this period of rapid cerebral expansion (Schulz et al., 1961; White et al., 1991). These figures reveal that the requirements of brain growth are trivial relative to cerebral energy needs and account for a small fraction of the body's total growth expenditure during this period. As shown in Table 3, most of the mass of the brain is water, with fat and protein accounting for only about 9.4% (44.5 g) and 10.1% (47.7 g), respectively, of brain growth during the first year of life. This represents only 3% of the 1,740 g of lipid and 6% of the 804 g of protein deposited in the growing infant body between birth and 12 months of age (male/female average from Fomon et al., 1982). Even in the adult, roughly 12% of brain weight is lipid, suggesting that the lifetime lipid requirement for brain growth contributes minimally to total body lipid deposition.

Brain size and the pattern of substrate use during starvation. Combined available data are more consistent with a perspective that views cerebral energy metabolism (Armstrong, 1983) rather than growth (Martin, 1981) as the predominant metabolic cost imposed by human encephalization and suggest that adipose tissue is more likely to serve as energy backup than growth buffer for the infant's large brain. However, is there evidence that fat stores are actually used to meet cerebral energy needs during a fast or, more importantly, that brain size influences reliance upon this resource during infancy? The brain is a glucose-using organ, and in the fed state most of the body's available glucose is devoted to cerebral energy metabolism (Cahill, 1982). That the human brain metabolizes substrate derived from adipose tissue during a fast was first demonstrated in 1967 by Owen and colleagues, who reported that ketones supplied 60% of cerebral needs in a group of semistarved obese volunteers. This finding reversed the traditional assumption that the brain must metabolize glucose for energy (see Keys et al., 1950), and it has since been shown that administering ketone bodies intravenously to infants or adults increases their uptake and use by the brain independent of circulating glucose, demonstrating that ketones are the preferred cerebral substrate in humans when their circulating concentration is elevated (Hasselbalch et al., 1996; LaManna and Lust, 1997). In contrast, ketones are not important energy substrates for the adult brain in fasting sheep, dog, or pig, and this has been related to the smaller cerebral energy requirements and smaller relative brain size of these species (Williamson, 1987). Along similar lines, Cahill (1982) has noted that the duration of survivable fast is increased by the small size of the brain relative to the body in such starvation-adapted species as polar bear, harp seal pups, and emperor penguins and has suggested that the thick fat layer of humans, including infants, might be explained in light of their unprecedented rela-

tive brain size and the energetic challenge that it poses during a fast.

Consistent with this perspective, there is limited evidence that the human infant's large brain forces heightened reliance upon fat stores. Fasting infants make the shift from carbohydrate to fat metabolism within 24 h without food, which is three to four times more rapid than the transition among adults and proportionate to their three to four times greater glucose requirements per unit body weight (Bier et al., 1977; Kerr et al., 1978; Saudubray et al., 1981). In turn, their greater metabolic rate is explained in large part by differences in the size of the brain relative to the body (Holliday et al., 1967), and this has been taken as evidence that the more rapid infant shift to reliance upon fat and fat metabolites for energy is a product of large brain size (Senior and Loridan, 1969; Bier et al., 1977). Kerr and colleagues (1978) demonstrated this rapid transition to fat use in fasting Jamaican infants studied before and after recovery from malnutrition and estimated that 92–94% of energy expended after 24 h without food was from stored fats, even for those initially malnourished. Despite the replenished fat stores of these infants in the well-nourished state, the authors calculated that the rapid rate of fat use during fasting conditions would deplete fat stores in 20 days, while usable protein would last twice as long (Kerr et al., 1978), leading them to conclude, "Availability of body fat as the major energy source is likely to be the most limiting factor in survival of infant malnutrition" (Kerr et al., 1978:412).

Why are humans fat at birth? Fat use at parturition and during late gestation. Thus, humans may need to enter the world fatter in order to ensure that the infant's high rate of energy use—itself largely explained by brain size—is buffered energetically against nutritional disruption. Indeed, postnatal life is initiated by an abrupt cessation of maternal nutritional support. At birth, the umbilical flow of nutrients is cut, and the newborn consequently must mobilize its own tissues to meet metabolic needs until the establishment of lactation, and fats deposited prenatally assume central importance as energy substrates during this transition (Greenberg, 1973). Circulating levels of free fatty acids and ketone bodies rise soon after birth, at which time the respiratory quotient has been observed to decline to 7.0, consistent with near-complete reliance upon fats for energy (Persson, 1969). Although linear growth typically continues unabated, this period is characterized by a reduction in fat mass (Largo et al., 1980; Elphick and Wilkinson, 1981) and a temporary decline in leptin levels (Marchini et al., 1998). Gampel (1965) has shown that newborns from postterm pregnancies—though increased in size relative to term and preterm babies—have relatively depleted fat stores at parturition, suggestive of placental insufficiency and fat mobilization. Thus, humans are forced to mobilize fat at birth and at times before to compensate for disruptions in the flow of maternal nutrients, and this could help explain why they begin fat deposition before birth.

The role of prenatal fat deposition as a mammalian strategy to prepare for postnatal energy stress is suggested by the fact that the few species known to deposit quantities of white fat in utero comparable to human infants, including the second and third fattest species (after humans) listed in Figure 1 (and plotted in Fig. 2), experience starvation or negative energy balance during the early postnatal period. This is true of harp seals, which are born with slightly less fat for their weight than humans (10% fat by weight) but proceed to lay down a massive layer during a brief 1 week suckling period in preparation for a postweaning fast that lasts a month or more (Bowen et al., 1985). The guinea pig is also born with 10% fat, which is mobilized after birth to compensate for the low energy content of breast milk and resultant "physiological undernutrition" (Widdowson and McCance, 1955:316). Thus, species that give birth to the fattest newborns on record share a common characteristic of being forced to mobilize and use this resource after birth.

While abrupt starvation and the composition of breast milk, respectively, underlie the energy shortage of newborn seal and guinea pig, studies linking relative brain size at birth to patterns of substrate use after partu-

rition provide limited evidence that brain size influences the magnitude of energy shortfall in the human newborn (Dawkins, 1964), as suggested above for infants. As the body's principle organ of glucose production and glycogen storage, the size of the liver relative to the brain is recognized as a primary determinant of susceptibility to glucose shortfall and thus resultant dependency on FFAs, glycerol, and ketone bodies (Wiggins et al., 1985), and it has been proposed that a higher ratio of brain size to liver size is a cause of the more common occurrence of hypoglycemia and ketosis among prematures (Dawkins, 1964). If correct, it follows that brain size (and liver size) is a determinant of the rate of fat mobilization and ketone body production among newborns and that having a larger brain (or smaller liver) is more likely to require use of fat stores for fuel. The role of brain size as a factor influencing reliance upon fat stores is further considered in subsequent sections as data permit, and other possible explanations for the prenatal onset of fat deposition are suggested. However, a more definitive test of the proposed link between relative brain size and adiposity awaits interspecific data on body composition and substrate use during a fast comparable to that available for human newborns and infants from species varying in relative brain size.

ADIPOSE TISSUE GROWTH DURING HUMAN INFANCY AND CHILDHOOD

Fat deposition in humans: Age changes and energy costs

Discussion thus far has affirmed that human newborns are fatter than expected for a mammal of their size and questioned whether the energy requirements of large brain size might shed light on this characteristic. Though born plump, human newborns do not attain peak adiposity until early infancy and subsequently experience a dramatic decline to a comparably lean condition by 5 years of age (Fig. 4). Estimates of body composition derived from predictive equations from skinfolds and indirect calorimetry reveal that roughly 40–65% of total body weight gain during the first 4–6 months of life is accounted for by fat deposition

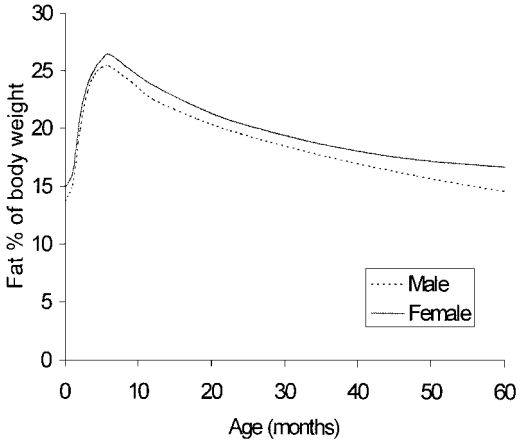

Fig. 4. Developmental changes in body composition during infancy and childhood represented as the fat percentage of body weight. Humans are fat at birth, experience a postnatal adiposity peak during infancy, and a subsequent decline to a leaner childhood. Based upon Fomon et al.'s (1982) reference body composition estimates.

(Fomon et al., 1982; Davies, 1992), and in well-nourished populations infants have typically reached a postnatal adiposity peak of approximately 25% fat by 6–9 months of age (Fomon et al., 1982). This depositional process accounts for most of the total cost of growth during early infancy. By reference to body composition data from Fomon et al. (1982) and published estimates of the energy costs of fat and lean tissue deposition in humans (Roberts and Young, 1988), it may be estimated that 72% of the approximately 20,000 Kcal necessary for tissue formation is accounted for by lipid deposition, with the remaining 28% spent on digestion, synthesis, and deposition of protein in lean tissue (Table 4). In Figure 5, the same data are used to estimate the monthly caloric investment in adipose tissue during the first 5 years of life (male/female average), showing the concentration of this energetic burden during the immediate postnatal period and the abrupt decline in investment in fat deposition during later infancy and childhood. As investment in the tissue is reduced, the fat proportion of body weight begins a gradual decline, eventually reaching a prepubertal nadir between 5 and 7 years of age of roughly 13% for males and 16% for females (Fomon et al., 1982).

TABLE 4. Fat and protein deposition as percentage of the total cost of growth in humans, birth to 6 months of age

	Gain (g)[1]	KJ/g[2]	Cost (KJ/KJ)[3]	Total cost (KJ)	% total
Male					
Fat	1,551	38.7	1.17	67,239	71.6
Protein	506	23.6	2.38	26,679	28.4
Total	2,057			93,918	100
Female					
Fat	1,420	38.7	1.17	64,342	72.1
Protein	444	28.6	2.38	24,939	27.9
Total	1,864			89,281	100

[1] Estimated weight gain from birth to 6 months of age (US data) from Fomon et al. (1982).
[2] Figures for gross energy in deposited fat and protein from Roberts and Young (1988). Note: 1 Kcal = 4.186 KJ.
[3] KJ spent in synthesis of each KJ in tissue. Total energy cost of protein and fat deposition = gross energy in tissue + energy used in deposition. From Roberts and Young (1988).

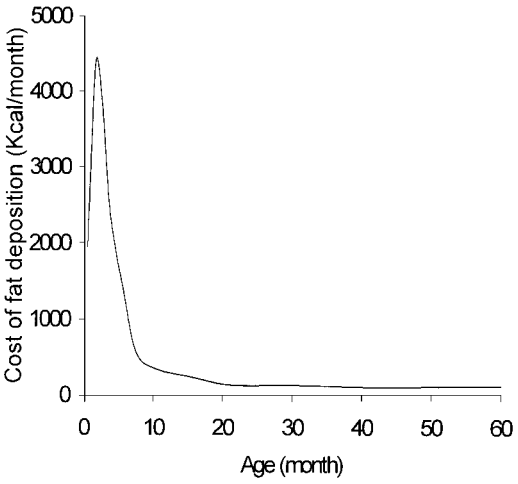

Fig. 5. Energy cost of fat deposition during the first 5 years of life expressed as kilocalories per month, male/female average. Energy invested in fat deposition is concentrated into the early postnatal period, after which fat deposition is minimal. Calculated using body composition data published by Fomon (et al., 1982) and estimates of the energy costs of fat deposition from Roberts and Young (1988).

Fat mass as independent variable: "Target-seeking" in fat growth

A pattern of adipose tissue growth similar to that described above has been documented in a wide range of well-fed human populations, although more commonly indexed by the correlated measures of skinfold thickness (see Tanner and Whitehouse, 1975; Eveleth and Tanner, 1976, 1990). Explanations for the growth trajectory of adipose tissue—which is driven by intensive infant investment followed by near-complete cessation of fat deposition during later childhood—are more rare and generally refer only to concurrent changes in the proximate determinants of energy balance, such as dietary intake and physical activity (Widdowson, 1974; Holliday, 1986; Lowrey, 1986). In his tome *On Growth and Form*, D'arcy Thompson (1942:119) stated this perspective most succinctly, noting, "The infant stores up fat, and the active child 'runs it off again.' " This view is echoed in a recent review of energetics, growth, and body composition (Holliday, 1986:108), which notes that during the second postnatal year, "as infants turn their attention from eating and growing to walking and playing, the percentage of fat decreases." Yet, as Garn (1956:246) has emphasized, "the truism that fat represents the difference between energy input and energy output does not explain how appetite and growth are synchronized to facilitate the rapid accumulation and deposition of fat during early infancy." Indeed, studies of fat growth in both human infants and animal models reveal that adipose tissue growth is capable of self-correcting upon recovery from nutritional stress, suggesting that the level of fatness per se may be a target of the growing body. As one example from a closely related species, Coelho and Rutenberg (1989) assigned newborn baboons to one of three diets varying in caloric density and monitored subcutaneous skinfold thickness at various depots. Fat stores were reduced in the low-calorie group, but the medium- and high-calorie groups followed a common skinfold curve with comparable skinfold velocities. Upon return to ad libitum feeding, animals fed the low-calorie diet experienced rapid catch-up adipose tissue growth and eventually normalized both absolute skinfold thickness and skinfold velocity relative to normal and overfed peers.

The results of the baboon study hint at "target-seeking" tendencies in adipose tissue growth, similar to the more widely appreciated process of catch-up skeletal growth commonly observed upon removal of a growth-impairing stressor (Tanner, 1990). Human infants are known to adjust the

volume of formula consumed based upon its caloric density and composition (Fomon et al., 1969; Adair, 1984), and target-seeking in fat growth similar to that of Coelho and Rutenberg's baboons has been observed in studies of human newborns. Lean newborns tend to put on more fat than their initially fatter peers, leading to a convergence in adiposity after several postnatal months (Garn, 1956; Davies, 1980). Similarly, premature newborns often have reduced fat stores at birth for their gestational age, but these infants have been observed to experience a rapid pace of postnatal fat deposition, normalizing adiposity index (BMI) relative to reference data by 6 months of age (de Gamarra et al., 1987; Micheli et al., 1994). That the intake of these infants is heightened during the period of rapid fat deposition suggests that the energy required of adipose growth influences their appetite and intake (Micheli et al., 1994).

Trade-offs and the physiology of weight regulation

Taken loosely, these observations suggest that, as the body aims for a level of fatness that shifts with age, the caloric requirements of fat growth have the ability to drive appetite and intake rather than merely vice versa. For the nursing mother, the hearty appetite of her rapidly growing infant represents an energetic drain with fertility consequences—for instance, by increasing interbirth interval through lactational amenorrhea (Lee, 1997). As noted, most of the cost of growth at this age is accounted for by fat deposition, suggesting trade-offs between infant adipose growth and maternal investment in future offspring. Current understanding of the physiology of bodyweight regulation views fat mass as a centrally monitored resource that is maintained within limits through adjustments in appetite but also through modifications of expenditure across other systems and processes, such as linear growth (Campfield et al., 1996), suggesting that the decision to allocate energy to the deposition and maintenance of fat stores involves trade-offs within the infant body as well. It has long been appreciated by researchers and dieters alike that food restriction and weight loss are followed by a surge in appetite and a period of reduced physical activity which favor recovery of lost weight (Kennedy, 1953; Weigle, 1994). The concept of body weight set point has traditionally described this tendency of body weight to be maintained within a limited range through metabolic adjustments (Mrosovsky and Powley, 1977), and the physiology underlying this phenomenon has been clarified in recent years by the discovery of the hormone leptin (Zhang et al., 1994), a peptide synthesized in fat cells (adipocytes) and secreted into the bloodstream in proportion to the lipid content of the cell. Circulating leptin levels are highly correlated with fat mass and thus provide a feedback signal reflective of energy stores, allowing the arcuate nucleus of the hypothalamus and other cerebral centers expressing leptin receptors to regulate appetite, metabolism, and expenditure in a fashion that maintains fat stores within limits (Campfield et al., 1996).

Although leptin has been viewed as a pathway designed to ensure energy stores sufficient to survive starvation (Gura, 1997), circulating leptin levels regulate expenditure across diverse systems, suggesting an important role for the hormone in a more complex calculus balancing trade-offs between the benefits of energy storage and the costs incurred by diverting resources from other functions, such as growth, activity, and, in adults, reproductive function (e.g., Finch and Rose, 1995). For instance, *ob/ob* knockout mice—which are incapable of synthesizing bioactive leptin—are obese and less active and have reduced metabolic rate, fertility, body temperature, and growth rates and delayed reproductive maturation (Halaas et al., 1995; Chehab et al., 1997). Because their adipocytes are incapable of producing viable leptin, leptin-sensing centers in the hypothalamus fail to detect adequate body fat stores and continue to shunt resources away from these functions to foster excessive weight gain. Giving injections of intact leptin to *ob/ob* mice lowers their body weight, percent body fat, and food intake while increasing metabolic rate, temperature, and activity and speeding growth rates and reproductive maturation (Pelleymounter et al., 1995; Chehab et al., 1997).

Of course, caution must be emphasized when extrapolating findings in growing rodents to human infants. However, a recent study reported associations between leptin levels and both the metabolic rate and the level of physical activity in human children, which the authors interpreted as preliminary evidence that leptin may regulate energy expenditure in children in a capacity similar to that observed in animal models (Salbe et al., 1997). Human infants whose growth has ceased due to wasting and malnutrition have been observed to start linear growth only after a substantial and possibly relatively fixed threshold of body weight is regained during the recovery period (Walker and Golden, 1988; Waterlow, 1994). This finding is consistent with observations of leptin action in animal models and suggests that regaining fat stores is a priority of the body recovering from nutritional depletion and one possibly involving direct energetic trade-offs with linear growth.

Hypothesis 2: Developmental changes in adiposity parallel the likelihood of nutritional disruption. Combined, these studies suggest that fat growth follows a trajectory with a target and that attaining this target is likely to involve trade-offs with maternal reproductive capacity and also with processes within the infant body, such as growth or the level of physical activity. Proceeding from the assumption that a caloric investment as costly as infant adipose tissue is unlikely to be maintained within ontogeny unless it contributes to fitness, age-related changes in adiposity may reflect the shifting importance of body fat, with the metabolic drive to shunt energy into storage balanced against the costs associated with sequestering resources from use elsewhere in the body—or the mother's body. The rising rates of pediatric obesity in the US (Gortmaker et al., 1987) and the global problem of infant malnutrition (World Bank, 1993) underscore that adipose growth is not predetermined, which is not implied here. Rather, the second hypothesis explored in this review is that the general human trend of early postnatal adiposity peak and childhood adiposity decline commonly observed in adequately nourished infants and children reflects a target trajectory shaped by expectable developmental changes in the likelihood of requiring fat stores to offset energy deficits. To explore this hypothesis, the following sections consider ecological and maturational factors—in addition to brain size—that are likely to influence age-specific patterns of energy stress and thus which might enter the cost-benefit calculus determining the drive to shunt available energy into storage. This hypothesis is explored primarily by reference to patterns of energy stress and fat use in contemporary nutritionally stressed human populations, which are taken as rough proxies for past selective pressures, and the limitations of this approach and its underlying assumptions are considered separately at the end of the review.

POSTNATAL TRENDS IN NUTRITIONAL DISRUPTION

Do changes in relative brain size account for developmental changes in adiposity?

Given the importance of brain size as an influence on the metabolic rate in human neonates and infants (Holliday et al., 1967), changes in the size of the brain relative to the body during infancy and childhood could influence susceptibility to energy shortfall, which in turn might determine the size of fat stores required as energy backup. As a rationale for this hypothesis, it was previously shown that the more rapid transition of infants than adults to fat metabolism during a fast is proportionate to differences in metabolic rate and, by implication, relative brain size. This hypothesis appears not to hold, however, as age changes in body composition during infancy and childhood do not parallel changes in metabolic rate, at least not precisely. Basal metabolic requirements expressed as either metabolic rate adjusted for body surface area (Stini, 1981) or glucose expenditure per kilogram of body weight (Bier et al., 1977) are reduced only slightly by mid-childhood, suggesting that children continue to have high metabolic needs relative to their body size and thus might be expected to remain relatively susceptible to energy shortfall (Fig. 6). In fact, based upon

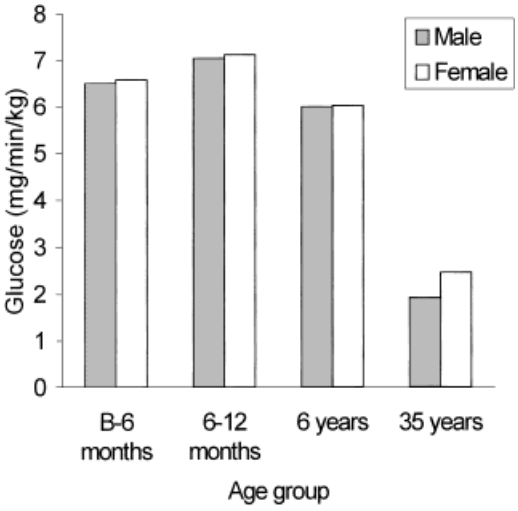

Fig. 6. Human metabolic expenditure at different ages expressed as glucose/kilogram/minute. Compared to infants, older children invest little in fat deposition despite continued high metabolic requirements, suggesting that they may be poorly equipped to survive a fast. Data from Bier et al. (1977).

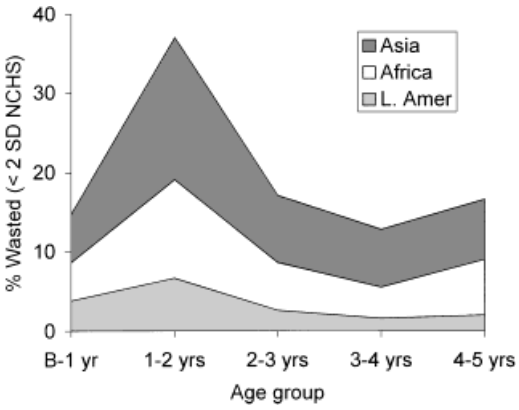

Fig. 7. Age changes in median prevalence of wasting by geographic region as indicated by a weight for height two standard deviations or more below the NCHS mean. Data from Keller and Fillmore (1983).

figures for body composition and metabolic rate, the estimated survival time from fat stores drops after 2 years of age and remains low until adulthood (Cunningham, 1995), a finding consistent with the observation that older children experience a greater increase and higher absolute mortality rates compared to infants during famine (Young and Jaspars, 1995). Thus, the size of energy backup declines more rapidly with age than do calories expended per kilogram of body weight, and this developmental trend appears to leave older children poorly equipped energetically to survive a fast.

Weaning

Older children are, however, far less likely to experience nutritional disruption than younger children and infants (Fig. 7), and this could help explain why they devote a small fraction of available energy to storage, even when well fed (Fig. 5). Infants are frequently cut off from nutritional support for reasons linked to their physically immature state, and older children have—for the most part—already successfully survived the brunt of this difficult period (World Bank, 1993). In particular, the transition from the nutritionally balanced resource of breast milk to supplemental foods of lower quality and the parallel transition from maternal to endogenous immune protection interact to increase the frequency and impact of nutritional disruption during infancy, and this effect is greatest at weaning (Dettwyler and Fishman, 1992). Although infant feeding practices vary widely across human populations, it is generally believed that exclusive breast-feeding is incapable of sustaining offspring growth beyond roughly 6 months of age in humans, and at this time, although in practice often before, breast milk must be augmented with supplemental foods to avoid growth faltering (Dettwyler and Fishman, 1992). Though necessary, supplementation is a two-edged sword, as introduced foods are often of poorer quality than breast milk but also expose the infant—whose immune system is yet immature (Cummins et al., 1994)—to food-borne pathogens that contribute to infections (Scrimshaw, 1989). As shown in Figure 8, the timing of peak infectious disease burden from common childhood infections like diarrhea roughly coincide with weaning age, as do associated mortality rates (Snyder and Merson, 1982). This graph demonstrates what is a common trend for most infectious diseases, with an early peak around weaning followed by gradual decline throughout later infancy and childhood (Galway et al., 1987).

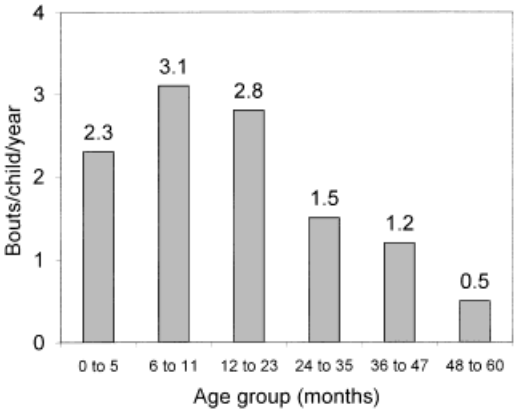

Fig. 8. Global median diarrheal episodes by age group from a metaanalysis by Bern et al. (1992).

The nutritional costs of infections are well-described, and are recognized as a primary cause of infant malnutrition and "under-five" mortality in contemporary populations in developing nations (Mata et al., 1972; Galway et al., 1987). In addition to the disrupted digestion and absorption of nutrients brought on by diarrhea (Rosenberg et al., 1977; Cole and Parkin, 1977), common micro- or macroparasitic infections also compromise infant nutrition by disrupting caretaker feeding practices (Chung and Viscorova, 1948), reducing infant appetite and intake (Briscoe, 1979; Martorell et al., 1980), and, in cases of severe febrile illness such as measles, increasing total energy needs (Du Bois, 1937; Stetler et al., 1992). Though the magnitude of effect may vary, the end nutritional result of infections generally lies in a similar direction, as the flow of nutrients from mother or environment is blocked from entry and use within the body (Scrimshaw, 1989). Moreover, nutritional stress is among the more problematic of disease symptoms, as it pushes children into a state less resilient against future infection (Pelletier, et al., 1993; Young and Jaspars, 1995). Through this vicious circle, infections and malnutrition contribute synergistically to deteriorating health and mortality, and in many poorer communities infants and young children experience cycles of infection and nutritional depletion that are causally intertwined (Mata et al., 1972).

Infection-malnutrition synergy, natural selection, and adiposity

The multiple pathways by which infections disrupt nutrient flow and the synergistic contribution of infections and malnutrition to mortality suggest that the high morbidity and mortality burden of weaning could select for a compensatory strategy of energy storage. To an infected infant, nutrients stored in body tissues provide an important edge over dietary nutrients in that their availability is independent of caretakers, appetite, gut physiology, and other critical links in the feeding process often disrupted during illness, and it may be for this reason that the human newborn allocates over 70% of growth expenditure to sustain a rapid pace of fat deposition during the first months of life (Fig. 5; Table 4). Consistent with this suggestion, epidemiologic studies of morbidity and mortality among infants and children from nutritionally stressed populations reveal that infants with adequate body tissue stores—as indicated by the commonly used weight-for-height index of nutritional status—have less severe infections and lower risk of mortality (Gibson, 1990). In prospective studies, children with low weight for height have been shown to have diarrheal bouts of longer duration and severity (Chen et al., 1981; Tomkins, 1981; Black et al., 1984; Rohde and Northrup, 1988; Black, 1993), and, less consistently, to suffer heightened risk of respiratory infections, including measles and pneumonia (Tupasi et al., 1990; Vathanophas et al., 1990; Victora et al., 1990). While a relationship between severe wasting and infectious mortality has long been recognized for infants (Chen et al., 1980), the importance of the more ubiquitous mild to moderate malnutrition as a potentiating influence in infection-related mortality has recently been emphasized by nutritionists. For instance, a recent analysis of data on mortality and nutritional status from 53 countries estimated that 56% of infectious disease mortality was attributable to malnutrition's potentiating effects, with 83% of these deaths associated with mild to moderate malnutrition (Pelletier et al., 1993). Similar associations between nutritional status and infectious mortality were

reported in an analysis limited to prospectively collected data (Schroeder and Brown, 1994).

Possible mechanisms: Is body fat protective during infection? These relationships should be viewed with caution, as they are potentially confounded by unmeasured biological and social factors and—for the purposes of the present discussion—are incapable of distinguishing the independent contribution of fat and protein stores to immune status or survival in infected infants. Claims for causal relationships must be backed, at a minimum, by a plausible mechanism, and in the present case the evidence is mixed. Although nutritional status is known to contribute directly to immune function (Chandra, 1994), the role of adipose tissue lipids during the energetic stress of infection is rarely discussed in this literature (e.g., Scrimshaw, 1989). This is likely explained, for one, by the fact that the metabolic response to the anorexia of infection—relative to that triggered by uncomplicated starvation—is characterized by reduced utilization of stored lipids for fuel and negative nitrogen balance, as amino acids are mobilized en masse for synthesis of immune factors, such as immunoglobulins and acute phase proteins (Scrimshaw, 1989). As such, the metabolic response to the negative energy balance of infections is not directly comparable to that of starvation, during which lipid mobilization minimizes lean tissue loss (Biesel, 1975). Second, unlike fats, which may be depleted without harm, amino acids are mobilized from tissues or organs, leading to functional deficits (Masaro, 1977), and are also more calorically costly to replace than depleted fats during recovery (Duggan and Milner, 1986). Finally, the possibility has been raised that immune function is impaired in obese adults (Stallone, 1994).

Nevertheless, clinical investigations—mostly of adults—reveal that stored fats are mobilized to meet energy requirements during infectious processes through the lipolytic action of hormones such as cortisol, growth hormone, and glucagon (Biesel, 1975). Whole body lipolysis is also one of a suite of metabolic and physiological responses triggered by cachectin (tumor necrosis factor), an important mediator of such processes involved in childhood infection as fever, inflammation, and anorexia (Tracey and Cerami, 1992). Release of stored fats by cachectin is viewed as one facet of a broader strategy of mobilizing substrates and energy from the periphery to sustain the requirements of activated immune defenses and immune factor synthesis in the liver (Tracey et al., 1989). Ketosis—indicating fatty acid mobilization and use—is commonly reported in infants suffering infections such as acute gastrointestinal infections (Hirschhorn et al., 1966) or respiratory infections complicated by vomiting (Nitzan et al., 1968). Even when production of ketones from free fatty acids is attenuated, fatty acids may enter directly into tissues capable of oxidizing them, such as muscle (Biesel, 1975), and septic patients receiving parenteral nutrition have been observed to experience metabolic alterations that preferentially favor fat oxidation in some infectious states (Carpentier et al., 1979; Askanazi et al., 1980; Schneeweiss et al., 1992).

Adipose tissue and lipolytic products also contribute directly to several facets of host defense, hinting at additional linkages between fat stores and immunocompetence. Pond and Mattacks (1995) report interactions between lymph nodes and surrounding fat depots, and they hypothesize that the anorexia associated with infection may serve to stimulate lipolysis in these depots, producing a mix of fatty acids appropriate for the nutrition and control of host defenses. Stored fats also contribute directly to fever as the substrate for nonshivering thermogenesis in brown fat (Cooper, et al., 1989) and shivering thermogenesis in skeletal muscle, and it has been hypothesized that the hyperlipidemia associated with infections is a component of the acute phase immune response, functioning to decrease toxicity of bacteria and viruses while redistributing nutrients to cells crucial to host defense (Grunfeld and Feingold, 1996). These studies raise the possibility of a more direct contribution of stored fats to resilience against infection.

Thus, there are at least plausible mechanisms that might link body fat stores with improved survival among infected infants,

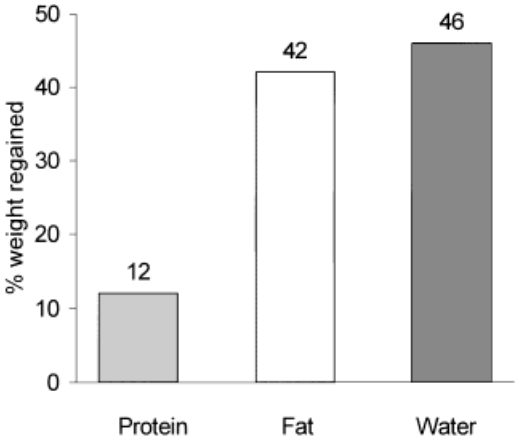

Fig. 9. Composition of weight gain in Jamaican infants recovering from protein calorie malnutrition revealing that fats are mobilized en masse in malnourished infants. Fat, protein, and water are expressed as a percentage of body weight gain. Data from Fjeld and Schoeller (1988).

which in turn could help explain relationships between weight-for-height and reduced infectious mortality. That these or some similar mechanisms do mobilize fat stores during infection and malnutrition is revealed by studies of the composition of weight regained by children recovering from these conditions. As illustrated in Figure 9, estimates of the fat percentage of weight gain in infants recovering from malnutrition range from 30–50% fat, with much of the balance represented by water (Spady et al., 1976; Fjeld and Schoeller, 1988). In a longitudinal study, Eccles et al. (1989) collected frequent measures of anthropometrics in relation to infections in Gambian infants followed as case studies and demonstrated acute shifts in the skinfold thickness z-score, consistent with cyclical mobilization and use of lipids to offset the energetic stress of recurrent infections (Fig. 10). However, it is likely that the utility of fat stores to a sick infant varies by virtue of the type of infection. For instance, the form of protein-calorie malnutrition known as kwashiorkor may be precipitated by acute infections, such as measles, and is often associated with well-preserved adipose tissue stores (Waterlow and Payne, 1975). In contrast, prolonged, chronic infectious states such as gastroenteritis are more commonly associated with marasmus, a form of severe protein-calorie malnutrition characterized by depleted—and thus used—fat stores (Waterlow and Payne, 1975).

Weaning and "fat faltering" in nutritionally stressed populations. At the population level, studies including measures of skinfold thickness provide evidence that fat stores are mobilized and used at weaning to buffer nutritional and infectious disease stress. Infants and children from nutritionally stressed populations tend to rapidly lay down fat for the first months of life, while breast-feeding protects and is adequate to sustain growth (Eveleth and Tanner, 1990). With the introduction of supplementary foods and its associated food-borne pathogen exposure, usually between 3–6 months of life (Dettwyler and Fishman, 1992), skinfold curves in such populations have been observed to falter from healthy norms (Fig. 11), often followed by a rebound and recovery of skinfold thickness with a temporary positive crossing of reference centiles later in childhood (Eveleth and Tanner, 1976; Eveleth, 1986; Eveleth and Tanner, 1990). While most studies reporting skinfold data on infants group data by year or half-year intervals, studies reporting more frequently collected skinfold measurements during the first few years of life have documented this pattern of early fat faltering in West Africa (Rea, 1971; Janes, 1974; Whitehead and Paul, 1984), North Africa (Boutourline et al., 1973), the Caribbean (Gurney et al., 1972), New Guinea (Malcolm, 1969), Latin America (Malina et al., 1974), the Middle East (Serenius and Swailem, 1988), South Asia (Brown et al., 1982), and Central Europe (Buzina, 1976), suggesting that it is relatively consistently observed in nutritionally stressed populations when measurements of sufficient frequency are available.

To illustrate the relationship between the weaning peak in infectious morbidity and fat depletion, Figure 11 shows triceps and subscapular skinfold thickness by age group reported for a rural Guatemalan community (Malina et al., 1974) presented with data from a separate report on diarrheal prevalence from the same population (Martorell et al., 1975). The authors attributed the

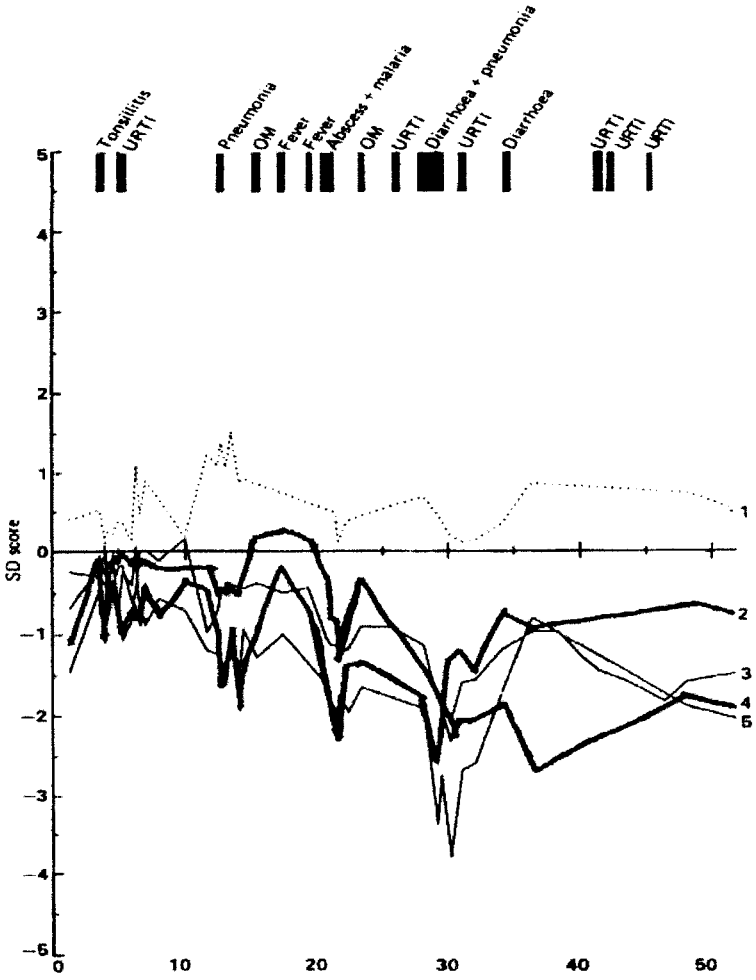

Fig. 10. Changes in z-score of frequently measured anthropometrics in a single Gambian child with concurrent infections listed across the top (OM, otitis media; URTI, upper respiratory tract infection). Dark lines are triceps and subscapular skinfolds (1, length; 2, subscapular skinfold; 3, weight; 4, triceps skinfold,; 5, mid upper arm circumference). The recurrent nutritional stress of infectious disease is associated with cyclic depletion and replacement of adipose tissue stores. (Reprinted from Eccles et al., 1989, with permission.)

depression in skinfold thickness to weaning, noting the poorer quality supplemental foods introduced at this time (Malina et al., 1974), and viewing data from both reports together suggests that diarrhea may also contribute to fat faltering in this population. The age of peak diarrheal incidence coincides with most rapid skinfold depletion, and the subsequent rebound in skinfolds occurs at an age of reduced diarrheal disease. Figure 12 plots the skinfold data from the Guatemalan population as a velocity curve in centimeters per month, demonstrating the initially rapid rate of fat deposition at both skinfold sites, the subsequent period of negative velocity—indicating fat mobilization—and finally the recovery of a positive skinfold velocity later in childhood. This crude association is incapable of establishing the relative importance and causal linkages among dietary changes, diarrhea, and changes in energy status, which are likely intertwined synergistically, but the extended period of negative fat velocity is consistent with mobilization of lipid deposited during the first 3 months of life to buffer the nutritional stress of weaning, to which infections contribute in this community (Martorell et al., 1980).

Form and function in postnatal adipose tissue growth

Comparing morbidity and adiposity in this population to adipose tissue development in the well-nourished cohort used as a reference in this review (Fig. 4) provides an opportunity to summarize and speculate on

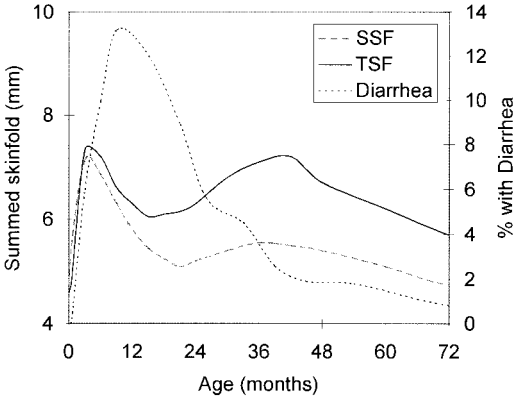

Fig. 11. Male/female average triceps (TSF) and subscapular skinfold (SSF) thickness in a rural Guatemalan community plotted with separately published data on diarrheal prevalence (male/female average) from the same population. This faltering of skinfolds—suggestive of fat mobilization and use—is commonly observed in nutritionally stressed populations when frequent measurements are available and coincides developmentally with the onset of weaning and peak diarrheal prevalence in this population (see Fig. 12). Skinfold thickness data from Malina et al. (1974). Diarrhea prevalence data from Martorell et al. (1975).

the functional basis of postnatal trends in adipose tissue growth during infancy and childhood, as posited in hypothesis 2. The age of peak fatness in healthier cohorts coincides with the trough in the population fat curve observed in this Guatemalan population (Fig. 11) and with peak risk of infectious disease, malnutrition, and fat faltering in similar communities more generally (Figs. 7, 8). Thus, well-fed and healthy infants appear to build up their largest body fat reserves by an age characterized by greatest fat reserve depletion, disease risk, and malnutrition in less-buffered contexts, and the subsequent reduced investment in the tissue by later childhood coincides developmentally with attenuated risk of these nutritional stressors. One interpretation of this concordance is that weaning stress—and age-specific trends in infection, malnutrition, and related mortality more generally—have influenced the pattern of energy investment during infancy and childhood, favoring a strategy that sequesters resources in preparation for future deficits when potential paybacks are high. As children mature, multiple factors improve resilience against infection and nutritional insult, suggesting that such payoffs are likely to decline with age. In particular, the risk of infectious disease, malnutrition, and mortality diminish with maturation of host defenses, including acquisition of an expanding repertoire of "memory" antibodies and T cells targeted specifically to locally encountered pathogens (Cummins et al., 1994) and maturation of the barrier defenses of the gut (Milla, 1986). From this perspective, the reduced capacity of older children to survive a fast as indexed by body fat stores, discussed earlier, is seen to match the attenuated likelihood of having to draw upon this resource to meet energy needs.

LIMITATIONS OF THE PROPOSED MODEL AND ALTERNATIVE EXPLANATIONS

This review develops an adaptive explanation for the abundance of adipose tissue at birth and its pattern of growth during human infancy and childhood, and assessing the relative merits of this hypothesis against others—such as the common insulation hypothesis—is no straightforward task; indeed, defining *adaptation* is itself a matter of controversy among evolutionary biologists (e.g., Gould and Lewontin, 1979). The proposed model is supported by evidence that body fat stores are mobilized and used by infants and children to offset energy stress, which likely acts as a strong agent of selection due to its powerful contribution to prereproductive mortality rates (Williams, 1957). The model is further supported by the finding that the age-specific pattern of investment in the tissue appears roughly suited to its shifting utility as energy buffer. In theory, there is a rationale to consider the adipose tissue of human neonates and infants as functional, as costly traits are rarely maintained unless they contribute to fitness. The trade-offs required of fat deposition for both infant and mother were highlighted previously, and sex differences in body composition in most mammals (McFarland, 1997), including human infants (Fig. 4), suggest that there are pathways available to modify investment in the tissue. Nonetheless, the model and its underlying assumptions warrant further scrutiny.

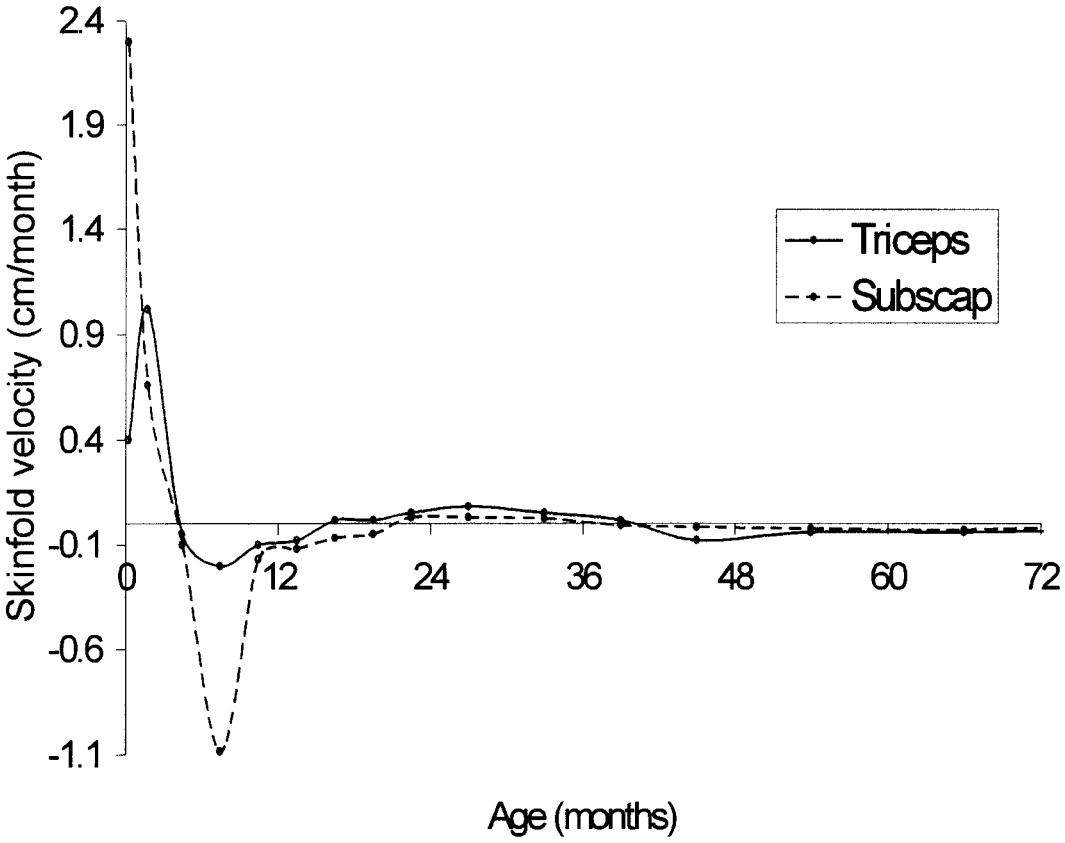

Fig. 12. Male/female average triceps and subscapular skinfold thickness velocity (cm/month) from a rural Guatemalan community. The period of negative skinfold velocity suggests mobilization of fat stores deposited during the first postnatal months to offset the energetic stress of weaning (see Fig. 11). Data from Malina et al. (1974).

Using current patterns of malnutrition, morbidity, and mortality as proxies for evolutionary selective pressures

The model assumes that contemporary developmental schedules of infectious disease, nutritional stress, and mortality in developing countries provide a rough approximation for selective pressures operating in infancy and childhood in recent evolutionary history and are thus a guide to what the body is likely adapted to. The pattern of fat growth in better-nourished populations is conversely interpreted as the body's target and the full or possibly even exaggerated expression of evolved responses to this stage of peak energetic stress made possible by nutritional abundance. On the one hand, it is likely that weaning and its associated nutritional stress has had ample opportunity to select for protective capacities, such as enhanced energy storage, given that nutritional stress and heightened susceptibility to infection are not unique features of human weaning but characteristic of mammals generally (Hart, 1990). Although not focusing on weaning per se, Debyser (1995) has compiled data on mortality in wild and captive primates and reports that infectious diseases are the major cause of infant and juvenile mortality among wild populations of great apes.

It is probable, however, that patterns of infant morbidity, malnutrition, and mortality observed in poorer populations in developing nations today (as reviewed above) are more severe, or qualitatively different, than weaning stressors before the rise of sedentary villages, which are believed to have

increased the burden of infectious disease and nutritional stress among the young (Cockburn, 1971; Cohen and Armelagos, 1984). If so, infection, malnutrition, and their synergistic interaction may have operated as strong agents of selection—akin to their current contribution to infant mortality rates in developing countries or to mortality rates in industrialized nations as recently as the turn of the century (reviewed in Bart and Lane, 1985)—for 10,000 years or less, depending upon region, and whether this has allowed sufficient time for modification of the pattern of human body fat growth is unclear. There is limited evidence for human evolutionary responses to ecologic factors on a similar time scale. Human populations show evidence for morphological adaptation to climate that is believed to be at least partially genetic in origin (Eveleth and Tanner, 1976), and some of this variation likely arose during recent prehistory (e.g., in the Americas), suggesting that adaptive modification of growth patterns may evolve relatively rapidly. The geographic distribution of the sickle-cell hemoglobinopathy in West Africa—a genetic trait that protects heterozygous carriers against malarial mortality—has been linked to patterns of land use and agricultural subsistence that affected the breeding habitat of the malarial vector (Livingstone, 1958), which is evidence that infectious mortality has contributed to adaptive genetic change in human populations on a historic timescale (Haldane, 1949). One testable hypothesis suggested by the present model is that—holding current proximate factors such as diet or physical activity constant—contemporary population differences in adipose tissue growth will trace to regional differences in the strength of nutritional and infectious stress as a force of selection (e.g., with contemporary populations whose ancestors were subjected to a historically protracted or more severe burden of infant infection or malnutrition attaining larger fat reserves in the months preceding weaning).

Nonadaptive explanations

Another possibility is that the pattern of fat growth in humans—which is distinguished by its prenatal onset of deposition—reflects the outcome of a developmental constraint (i.e., a necessary by-product of selection on some other aspect of ontogeny) (Gould and Lewontin, 1979). If so, the match between current patterns of investment in the tissue and use of fat stores, as highlighted in this review, may merely reflect the fortuitous use of a trait that did not evolve to serve its present function. For instance, primates have longer gestational periods than other mammals of their size (Harvey et al., 1987), and it is thus possible that the prenatal onset of fat growth in humans, though often useful to newborns at parturition today, was a necessary outcome of extending gestation. Several features of primate and human maturation argue against this hypothesis. For one, the other great apes also have extended gestation but as noted, appear not to deposit significant quantities of body fat prenatally (Schultz, 1969), although this assertion awaits to be confirmed with better data. Consistent with hypothesis 1 presented above, Leonard and Robertson (1994:186) estimate that humans devote 3.5 times the calories to the brain as predicted for an anthropoid of human body size, from which they conclude that "even relative to other primate species, humans are distinct in the proportion of metabolic needs for the brain."

By the criteria of skeletal ossification centers, humans are also born altricial compared to other mammals and primates (Watts, 1990), and human encephalization itself may have required a paedomorphic (neonatal) extension of fetal growth processes into later life coupled with a delay of maturation (Gould, 1977). As suggested, this makes the prenatal onset of human fat growth more remarkable, as most mammals—including those born in a more advanced maturational state—do not begin to deposit significant quantities of fat until after birth (Adolph and Heggeness, 1971). Although more data on nonhuman primates are necessary to clarify this, the shift in timing of fat deposition to the prenatal period in humans is thus unlikely to be explained as a coupled outcome of paedomorphosis. In her comparative studies of primate growth and maturation, Watts (1990: 101) has shown that the rate of maturation of different systems—such as the dentition, skeletal, and reproductive systems—have

been free to evolve relatively independent of one another in the course of primate evolution and suggests that "selection may have operated differently on the various functional systems." The fetal onset of adipose tissue growth in the otherwise altricial human newborn may be a case in point.

It is also notable that the prenatal trajectory of body fat growth roughly parallels that of fetal brain growth (Fomon, 1966; Dobbing and Sands, 1973), and the period of peak postnatal fat deposition is also one of continued rapid brain growth and myelination (Wiggins et al., 1985). It is thus possible that the process of substrate deposition in the developing central nervous system is linked physiologically to that of fat deposition. This too seems unlikely, however, as most species do not begin to deposit white fat until after parturition (Adolph and Heggeness, 1971; Schultz, 1969), when the majority of brain growth is complete (Passingham, 1985). The present model posits that the large brain of the human newborn requires an earlier onset of fat deposition to ensure adequate energy reserves to buffer the nutritional disruption of parturition. This focus upon the tissue's role as backup for brain energetics—rather than growth—followed from the finding that cerebral energy metabolism accounts for most of the nutritional burden associated with encephalization (indeed, most of metabolic rate), with substrate deposition associated with brain growth accounting for a comparably trivial fraction of the body's growth expenditure.

Selection for heightened adiposity may be limited to a specific stage of development, which could influence the level of adiposity at other ages for reasons of pleiotropy rather than function. For instance, selection to increase postnatal adiposity, perhaps at weaning or as insulation, might require a shift of the entire fat growth curve into earlier, and thus fetal, development. Increased adiposity of human newborns relative to other species would be a necessary by-product of such selection. However, the finding that fat stores are depleted in some late-term pregnancies and the well-known newborn reliance on fats at parturition suggest that prenatally deposited fat is frequently mobilized and used at or before birth. Moreover, as noted, the common occurrence of malnutrition after weaning suggests that energy is typically in short supply postnatally in less-buffered contexts, from which it was inferred that the drive to amass fat stores in the well-fed infant is similarly not without purpose. The energetic hypothesis presented here—like the insulative hypothesis common in the literature—provides one testable explanation for the trends observed, but other possible explanations undoubtedly exist and should be considered.

CONCLUSIONS AND PREDICTIONS

It was shown that human newborns have a fat mass roughly four times that predicted for a mammal of their body size at birth, which is a significant divergence from the best-fitting trend and consistent with past assertions that humans enter the world well-endowed with fat stores. Although published observations among primates suggest that they begin to deposit white fat postnatally, as do most mammals, further data on nonhuman primate body composition at birth are necessary to clarify more definitively whether human newborns are a fat primate or merely a fat mammal for their size at birth. Explanations for the ponderous condition of human newborns have typically assumed that the abundance of body fat evolved as compensation for the human lack of an insulating fur, which is rare among mammals and unique among primates. Yet review of the literature on human adaptation to cold and human neonatal thermoregulation revealed only weak evidence for a role of subcutaneous fat in adaptation to cold stress in humans, including neonates and infants, and this hypothesis thus awaits empirical support.

The energy storage function of body fat has received little consideration as an explanation for its abundance in early human development, yet human infants face energetic challenges that are as unique in comparative perspective as their hairlessness. Humans are unsurpassed among mammals for which data are available in the size and energetic cost of their brain, and this feature is pronounced during infancy, when the brain consumes an estimated 50–60% of the body's

available energy. The energy requirements of the human brain have been hypothesized previously as having necessitated evolutionary shifts to greater maternal investment in offspring or outside assistance in offspring provisioning and as having required an energetically denser diet, changes in foraging practices, and less expenditure on linear growth (Foley and Lee, 1991; Leonard and Robertson, 1992, 1994; Bogin, 1997). From the infant's perspective, devoting most of total metabolic output to an organ with inflexible needs and one that may increase total caloric requirements relative to body size compared to closely related taxa (Foley and Lee, 1991), has likely selected for the ability to sustain this energy need when the flow of nutritional support from mother or other caretakers is cut, and it was hypothesized that fat stores have been augmented in human offspring to serve this function.

The data reviewed provide support for this hypothesis, albeit only indirectly. Studies of substrate use among fasting infants reveal a precarious balance between demand for carbohydrate and its supply and a critical role for fats stored in adipose tissue to compensate for energy deficits. That the metabolic transition from carbohydrate to fat metabolism is sped up in infants relative to adults in proportion to their greater metabolic rate—which in turn is largely a product of greater cerebral requirements—is evidence that brain size is a factor influencing reliance upon stored fats for fuel in human infants. There is similar evidence that large relative brain size at birth predicts hypoglycemia and hence compensatory requirements for free fatty acid and ketones. These findings are consistent with a role of relative brain size as a determinant of reliance upon fat stores in human infants, but test of this hypothesis awaits interspecific data on substrate use during a fast comparable to that available for humans—for instance, documenting how rapidly the shift to fat use occurs after a fast and the rate of fat mobilization.

Devoting energy to storage is itself a costly enterprise requiring trade-offs with other functions within the infant body but also with maternal energetics and thus fertility correlates, such as interbirth interval. Following from this observation, the second hypothesis explored in this review proposed that developmental changes in the pattern of investment in body fat would be—roughly speaking—proportionate to expectable payoffs from energy reserves (i.e., the likelihood of experiencing energy stress). Human neonates are forced to mobilize and use prenatally deposited fats for energy at parturition and until lactation is established, and fat stores may also be important at times in utero, as late-term births are often associated with depleted fat stores, suggesting their mobilization and use to compensate for placental insufficiency (Gampel, 1965). The prenatal onset of fat deposition in humans may thus be necessary to buffer the disrupted nutrient flow that commonly accompanies the transition from placenta to breast, a suggestion supported by the finding that the second and third fattest species at birth—after humans—are also forced to mobilize this resource at or soon after parturition. Whether the earlier onset of fat deposition of humans might be explained as a correlated outcome of selection on other developmental processes was briefly considered, but it was noted that the precocious maturational timing of adipose tissue deposition runs counter to other evolutionary trends proposed for human ontogeny, such as paedomorphosis or maturational delay.

Weaning marks a second major nutritional transition, when the infant begins the difficult shift from reliance upon nutritionally balanced and sterile breast milk to solid foods, and continues the shift begun at birth from reliance upon maternal immune protection to endogenous host defenses. Both processes contribute to the increased frequency and severity of nutritional disruption at weaning, and the synergy between infection and malnutrition underlies a significant proportion of worldwide under-five mortality, suggesting its importance as a force of selection in early human ontogeny. That infectious mortality might favor a strategy of enhanced energy storage is suggested by evidence that plumper infants (as measured by weight-for-height z-score) have lower infectious morbidity and mortality and that fat stores are mobilized and used during infections as energy substrates but possibly

also in several more direct roles in host defense. It was estimated that healthy infants devote over 70% of growth expenditure to fat deposition during the first 6 months of life and thereby attain a state of peak adiposity by an age characterized by peak risk of malnutrition, infection, and fat depletion in less-buffered contexts. Healthy older children, in contrast, invest minimally in the tissue and are poorly equipped energetically to survive a fast as a result, but this reduced investment appears appropriate given their attenuated risk of infection, nutritional disruption, and associated reduced mortality risk relative to infants. Thus, malnutrition-related mortality schedules during infancy and childhood—which trace to factors that determine susceptibility to infection and nutritional disruption, such as the timing of weaning, the development of immunocompetence, and maturation of the gut—appear to help explain the pattern of investment in energy reserves. Another potentially relevant factor not considered is the self-sufficiency that older children attain with age, which reduces their reliance upon others for food and care (e.g. Hawkes et al., 1995), thus possibly attenuating the risk of nutritional disruption.

While sex differences were not foregrounded in this review, it is notable that females enjoy lower rates of malnutrition, infectious disease morbidity, and mortality at all ages (Stinson, 1985; World Bank, 1993). The model predicts that the greater susceptibility of males to nutrition-related mortality is at least partly explainable as a result of their smaller investment in energy storage and consequent reduced adiposity relative to females throughout the growing years (Fig. 4). This pattern is consistent with a trade-off between energy storage and other functions, such as linear growth or muscle mass, which are augmented in males (Tanner, 1990), and may have sufficiently large future fitness returns to offset the higher mortality associated with reduced energy storage during infancy. Similar predictions could be advanced to explain interspecific variation in adiposity and its relationship to other expenditures, such as growth, or to mortality schedules. It has recently been proposed that primate growth-rate and life-history variation relates to evolutionary differences in the risk of juvenile starvation, with species faced with high starvation pressure adopting slower and less costly growth rates (Janson and Van Schaik, 1993). The present model predicts that, as juveniles, such species will also devote a greater percentage of growth expenditure to storage in fat reserves than species faced with lower starvation risk.

Although use of fat stores for energy necessarily competes with the tissue's insulative qualities (Pond, 1997), there is no a priori reason to rule out additive selection across different environments relating to both energetic stress and climate. For instance, it may be that humans on average are fatter than other mammals to compensate for greater energetic needs during a fast, but selection associated with temperature stress may have augmented adipose mass beyond the tissue's energetic requirements to serve an enhanced insulative or thermogenic role among the long-term inhabitants of cold climates or higher latitudes. However, the proposed model predicts that population differences in adiposity or fat growth during infancy and childhood will relate more strongly to historical differences in selective pressures associated with energy stress than to climate, holding current proximates such as diet, infectious disease load, and activity constant.

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