In the same article, some 4500 words earlier, Feinstein refers to psychic stress as a possible risk factor for coronary disease. However, the reader should judge whether, in the above passage, Feinstein was referring to coronary disease or to lung cancer.

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Body Weight and Reproduction

Conclusions by J. E. Schneider and G. N. Wade (Reports, 16 June, p. 1326) about the control of reproduction of the Syrian hamster weighing 85 to 95 grams (3.0 to 3.3 ounces) when adult do not necessarily apply to women, as suggested in This Week in Science (16 June, p. 1231). For a woman weighing 57,000 grams (125 pounds) when adult 26 to 28% [16,000 grams (35 pounds)] is fat (*1*). Contrary to the conclusion by Schneider and Wade from the hamster data that "reproduction is controlled by the general availability of metabolic fuels, rather than by any dimension of body size," a large amount of data for women indicates that body size and composition are important to successful female reproduction (*2–7*). Fatter girls have menarche earlier than do thinner girls (*2, 8*). Menarche is delayed in very lean girls, sometimes to as late as ages 18 to 21 (*9*). Fatter women have a later age of menopause than do thinner women (*10*). Most important for fertility, it is well documented that when a woman loses 10 to 15% of her normal body weight, which is equivalent to a loss of one-third of her body fat, menstrual cycles and ovulation cease due to hypothalamic dysfunction (*2-7, 11*): the pulsatile release of gonadotropin releasing hormone (GNRH) becomes abnormal (*5, 6, 11*). The disruption is reversible: gain of weight restores normal GNRH pulsatile secretion, and thus fertility (*6*).

That a dimension of body size is important to the sexual maturity of women would be expected, since the survival of the human infant is correlated with birth weight; and birth weight is correlated with the prepregnancy weight of the mother and independently with her weight gain during pregnancy (*12*). Also, the caloric cost of a human pregnancy is about 50,000 calories, and lactation requires about 500 to 1000 calories a day. The main function of the 16,000 grams of stored female fat, equivalent to 144,000 calories, may be to provide energy for a pregnancy and for lactation (*2–4*). In prehistoric times, when the food supply was scarce or fluctuated seasonally, stored fat would have been necessary for successful reproduction, as Schneider and Wade recognize. Excessive fatness also disrupts reproductive ability in women, as it does in animals (*13*). Weight loss to the normal range results in the restoration of fertility.

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Response: The well-known correlation between fertility and body fat content has been heuristically valuable to many investigators, including us. We found the same correlation in Syrian hamsters. However, these correlations cannot be considered strong evidence for the hypothesis that reproductive status is directly determined by any single dimension of body size or composition. As we noted in our paper, the correlation between fatness and reproductive cyclicity is not always present, either in humans (*1*) or in rats (*2*).

More important, when tested directly, a critical fatness hypothesis is not supported. In Syrian hamsters, a particular body fat content is not necessary for the maintenance of estrous cycles as long as one or more metabolic fuels is supplied in the diet (*3, 4*). Conversely, a high body fat content is not sufficient for maintenance of estrous cycles when the availability of metabolic fuels is inhibited pharmacologically (*4*). The importance of the availability of metabolic fuels in the control of reproduction is supported by data from a wide phylogenetic range of species. In food-restricted, prepubertal male macaques, which normally have reduced circulating levels of luteinizing hormone (LH), LH levels increased after infusion with glucose and amino acids (*5*). The increase in LH was not correlated with body weight, weight gain, or age. In female rats in which puberty has been delayed by food restriction, LH pulsing characteristic of adults can be induced within 2 to 4 hours by allowing the animals to ingest a meal (*6*).

Thus, useful models relating nutrition and reproductive function must account for factors in addition to body weight and composition. A metabolic fuel hypothesis is consistent with the well-known correlation between fertility and body fat content, since adipose tissue is a storage depot for one of these fuels (fatty acids). There is no doubt that fatness and fertility are correlated. Nevertheless, it is conceivable that this correlation simply reflects the fact that both fuel storage in adipose tissues and reproduction require a supply of metabolic fuels over and above those necessary for maintenance of essential functions such as basal metabolism, thermoregulation, and locomotion.

With regard to Frisch's statement about whether it is appropriate to extrapolate conclusions in 85-gram hamsters to 57,000-gram humans, we hope that future research in this area will be guided by testable hypotheses based on strong inference rather than on purely correlational evidence, regardless of the body weight of the species studied.

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