## Menstrual Cycles: Fatness as a Determinant of Minimum Weight for Height Necessary for Their Maintenance or Onset

Abstract. Weight loss causes loss of menstrual function (amenorrhea) and weight gain restores menstrual cycles. A minimal weight for height necessary for the onset of or the restoration of menstrual cycles in cases of primary or secondary amenorrhea due to undernutrition is indicated by an index of fatness of normal girls at menarche and at age 18 years, respectively. Amenorrheic patients of ages 16 years and over resume menstrual cycles after weight gain at a heavier weight for a particular height than is found at menarche. Girls become relatively and absolutely fatter from menarche to age 18 years. The data suggest that a minimum level of stored, easily mobilized energy is necessary for ovulation and menstrual cycles in the human female.

The cessation of menstrual cycles (amenorrhea) following chronic undernourishment or rapid weight loss in otherwise normal women is a welldocumented (1, 2), although often overlooked, fact of human reproductive physiology. Amenorrhea also accompanies the self-inflicted starvation of anorexia nervosa, a psychogenic disease most prevalent among adolescent girls (3, 4). Undernutrition delays menarche (5) and the adolescent growth spurt, which normally precedes menarche (6). An increase in food intake and a gain in body weight restores normal menstrual function after varying intervals of time (1-4).

We report a simple method of estimating a minimal weight for height necessary for the onset of menstrual cycles (menarche) in primary amenorrhea and for the restoration of menstrual cycles in cases of secondary amenorrhea when the amenorrhea is due to undernourishment.

We also report that women of ages 16 years and over with secondary amenorrhea resume menstrual cycles at a heavier weight for a particular height than is found at menarche. In accord with this finding, we show that normal girls become relatively and absolutely fatter from menarche to reproductive maturity at ages 16 to 18 years.

The method of estimation of the minimal weights for menstrual function is based on previous findings that menarche is associated with the attainment of an average critical body weight in populations of U.S. and European girls (5, 7-9). The average critical weight represents a critical body composition of fat as a percentage of body weight (10), which is attained at varying weights and heights within a population. For example, the shortest, lightest girls and the tallest, 13 SEPTEMBER 1974

heaviest girls at menarche have the same percentage of their body weight as fat, although they differ in height by about 20 cm and in weight by about 11 kg (11).

Two diagrams show a minimal weight for height for the onset of cvcles (Fig. 1) and a minimal weight for height for the restoration of menstrual cycles (Fig. 2). These diagrams were made by calculating the total body water as percentage of body weight (hereafter referred to as total water/ body weight percent), an index of fatness (12, 13), for each of 181 girls of three longitudinal growth studies at ages 14, 15, 16, and 18 years from the height and weight of each girl at each of those ages, as had already been done at menarche for each of the same girls (10)

Percentiles of total water/body weight percent, which are percentiles of fatness (14), were made at menarche and at age 18 years, the age at which we found body composition was stabilized. Each set of percentiles was then drawn on a height-weight grid (Figs. 1 and 2).

The weights at the cessation and restoration of regular menstrual cycles (two or more) of nine patients, mean age 21.7 years (range 16 to 27 years), with amenorrhea due to weight loss, other possible causes having been excluded, were studied in relation to the weights indicated by the percentile lines of Figs. 1 and 2, noting especially the weight at the cessation and resumption of menstrual cycles. The weights before and during amenorrhea of eight anorexic women, whose mean age was 23 years (range 16 to 30), reported by Lundberg et al. (4), were also compared with the standards in the same way.

We found that 56.1 percent of total water as percentage of body weight

(the 10th percentile at age 18 years), which is equivalent to about 22 percent fat of body weight, indicates a minimal weight for height necessary for the restoration and maintenance of menstrual cycles for women of ages 16 years and over.

Figure 2 shows that the body weight for her height of all but one amenorrheic patient was below the weight indicated by the 10th percentile of total water/body weight percent, and in each case, periods resumed after attainment of a body weight above that percentile.

The body weights of anorexic, amenorrheic Swedish women are also below the weights indicated by the 10th percentile line, whereas their original weights are all above that line; in fact, all but one are above the 50th percentile (Fig. 2).

The weights at which menstrual cycles ceased or resumed in postmenarcheal patients ages 16 and older (Fig. 2) are about 10 percent heavier than the minimal weights for the same height observed at menarche (Fig. 1).

In accord with this finding, the data on body composition show that both early and late maturing girls gain an average of 4.5 kg of fat from menarche to age 18 years. Almost all of this gain is achieved by age 16 years, when mean fat is  $15.7 \pm 0.3$  kg, 27 percent of body weight. At age 18 years mean fat is  $16.0 \pm 0.3$  kg, 28 percent of the mean body weight of  $57.1 \pm 0.6$  kg. Reflecting this increase in fatness, the total water/body weight percent decreases from  $55.1 \pm 0.2$  percent at menarche  $(12.9 \pm 0.1 \text{ years})$  (10) to  $52.1 \pm 0.2$  percent (S.D., 3.0) at age 18 years (15).

Because girls are less fat at menarche than when they achieve stable reproductive ability, the minimal weight for height for the onset of menstrual cycles in cases of primary amenorrhea due to undernutrition is indicated by the 10th percentile of fractional body water at menarche, 59.8 percent, which is equivalent to about 17 percent fat of body weight (Fig. 1).

The standards of Fig. 1 would be used also for girls who become amenorrheic as a result of weight loss shortly after menarche, as is often found in cases of anorexia nervosa in adolescent girls (16).

The weight changes associated with the cessation and restoration of menstrual cycles are in the range of 10 to 15 percent of body weight. Weight loss or weight gain of this magnitude is mainly loss or gain of fat (1, 17). This suggests that a minimum level of stored, easily mobilized energy is necessary for ovulation and menstrual cycles in the human female.

If a minimum of stored fat is necessary for normal menstrual function, one would expect that women who live on marginal diets would have irregular cycles, and be less fertile, as has been observed (18), and that poorly nourished lactating women would not resume menstrual cycles as early after parturition as well-nourished women, as also has been observed (18). The absolute and relative increase in fat from menarche to age 16 to 18 years is of interest because this interval coincides with the period of adolescent sterility (19). During this time there is rapid growth of the uterus and the ovaries (20). The main function of the 16 kg of fat stored on an average by both early and late maturers by age 18 years may be to provide easily mobilized energy for a pregnancy and for lactation; the 144,000 calories would be sufficient for a pregnancy and 3 months' lactation (21).

The findings on gain and loss of fat associated with the restoration and cessation of menstrual cycles fits with a postulated interaction between energy homeostasis and reproductive function (7-9, 11, 22).

Our standards apply as yet only to white U.S. females (23) and European females, since different races have different critical weights at menarche (6), and it is not as yet known whether the different critical weights represent the same critical body composition.

Other factors, such as emotional stress (24), affect the maintenance or onset of menstrual cycles. Therefore, menstrual cycles may cease without weight loss, and may not resume in some subjects even though the mini-

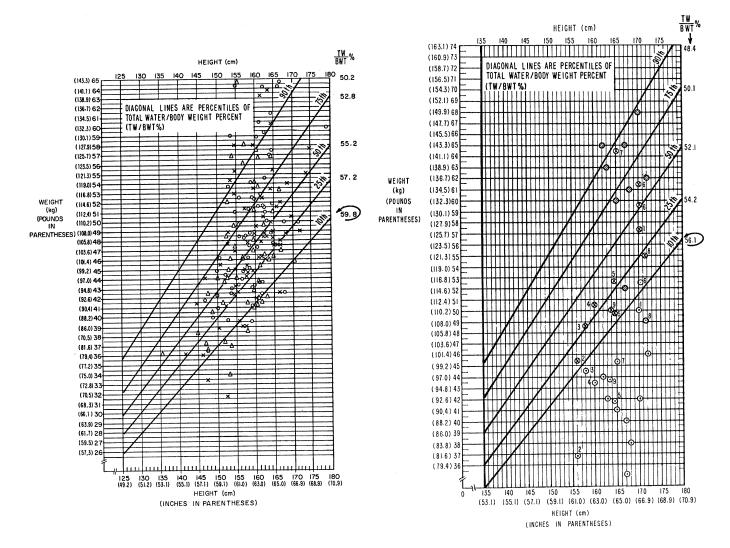


Fig. 1 (left). The minimal weight necessary for a particular height for onset of menstrual cycles is indicated on the weight scale by the 10th percentile diagonal line of total water/body weight percent, 59.8 percent, as it crosses the vertical height lines. Height growth of girls must be completed, or approaching completion. For example, a 15-year-old girl whose completed height is 160 cm (63 inches) should weigh at least 41.4 kg (91 pounds) before menstrual cycles can be expected to start. Symbols are the height and weight at menarche of each of the 181 girls of the Berkeley Guidance Study ( $\bigcirc$ ); Child Research Council Study (X); and Harvard School of Public Health Study ( $\triangle$ ) (7–9). Fig. 2 (right). The minimal weight necessary for a particular height for restoration of menstrual cycles is indicated on the weight scale by the 10th percentile diagonal line of total water/body weight percent, 56.1 percent, as it crosses the vertical height line. For example, a 20-year-old woman whose height is 160 cm should weigh at least 46.3 kg (102 pounds) before menstrual cycles would be expected to resume.  $\bigcirc^{1-9}$ . Weights while amenorrheic of patients of one of us (J.W.M.);  $\bigotimes^{1-9}$ , their weights at resumption of regular cycles. When two weights are given for a patient, the lower weight is at first resumed cycle.  $\bigoplus$ . The weights before occurrence of amenorrhea of subjects cited by Lundberg *et al.* (4), and  $\bigcirc$  are their weights while amenorrheic (4).

mum required weight is attained. However, this does not negate the finding that a critical minimum weight appears to be necessary for the onset and maintenance of normal menstrual cycles in the human female.

ROSE E. FRISCH

Harvard Center for Population Studies, Cambridge, Massachusetts 02138

JANET W. MCARTHUR

Department of Gynecology, Massachusetts General Hospital,

## Boston 02114

## **References and Notes**

- A. Keys, J. Brožek, A. Henschel, O. Mickelson, H. L. Taylor, *The Biology of Human Starvation* (Univ. of Minnesota Press, Minneapolis, 1950), vol. 1, pp. 749–763.
   S. Zubirán and F. Gómez-Mont, Vitam. Horm. 11, 97 (1953); R. Iizuka and S. Kawakami, Sanfujinka No Jissai (Tokyo) 17, 388 (1968); H. Fries and S. J. Nillius, Acta Psychiat, Scand. 49, 669 (1973). Amenorhea is primary when there is failure of menstruation primary when there is failure of menstruation
- primary when there is failure of menstruation to begin, and secondary when menstruation stops after having been established. A. H. Crisp and E. Stonehill, Br. Med. J. 3, 149 (1971); A. H. Crisp, World Rev. Nutr. Diet. 12, 452 (1970); A. Wakeling and G. F. M. Russell, Psychol. Med. 1, 30 (1970). D. O. Lundberg, L. Wälinder, I. Werner, L. 3.
- M. Russen, Psychol. Med. 1, 30 (1970).
  4. D. O. Lundberg, J. Wålinder, I. Werner, L. Wide, Eur. J. Clin. Invest. 2, 150 (1972).
  5. R. E. Frisch, Pediatrics 50, 445 (1972).
  6. (1970).
  6. (1970). (1969).
- 9. R.
- -, science 169, 397 (1970). , Arch. Dis. Childh. 46, 695 (1971). R. E. Frisch, R. Revelle, S. Cook, Science 174, 1148 (1971); R. E. Frisch, Lancet 1973-I, 1007 (1973).
- R. E. Frisch, R. Revelle, S. Cook, Human Biol. 45, 469 (1973).
   R. E. Frisch, in The Control of the Onset of Puberty, M. Grumbach, G. Grave, F. Mayer, Eds. (Wiley, New York, 1974). p. 403; Pediatrics 53, 389 (1974).
   R. I. Frije-Honsen, Acta Ragdigt 110 (Suppl.) 12. B. J. Friis-Hansen, Acta Paediat. 110 (Suppl.),
- 1 (1956). 13.
- I. S. Edelman, H. B. Haley, P. R. Schloerb, D. B. Sheldon, B. J. Friis-Hansen, G. Stoll, F. D. Moore, Surg. Gynecol. Obstet. 95, 1
- F. D. Moore, Surg. Gynecol. Obstel. 95, 1 (1952).
  14. R. E. Frisch, Pediatrics 53, 389 (1974). The percent fat is equal to 100 (percent water/0.72) [see (10, 13)].
- 15. Our calculated total body water and fat data are in accord with those from direct measurements of total body water for females of ages 20 to 31 years (13), and the data for lean ages 20 to 31 years (13), and the data for lean body weight and fat at age 18 years found from <sup>40</sup>K whole-body counting [G. B. Forbes, *Growth* 36, 325 (1972); G. R. Meneely, R. M. Heyssel, C. O. T. Ball, R. L. Weiland, A. R. Lorimer, C. Constantinides, E. U. Meneely, *Ann. N.Y. Acad. Sci.* 110 (part 1), 271 (1963)].
- M. P. Warren and R. L. Vande Wiele, Am. J. Obstet. Gynecol. 117, 435 (1973).
   M. Kleiber, The Fire of Life (Wiley, New York).
- York, 1961); see also (1), vol. 1, pp. 161-183.
- N. Solien de Gonzalez, Am. Anthropol. 68, 873 (1964); C. Gopalan and A. N. Naidu, Lancet 1972-II, 1077 (1972).
- 19. C. G. Hartman, Science 74, 226 (1913); National Academy of Sciences, Relation of Nutrition to Pregnancy in Adolescence; Nutrition to Pregnancy in Addescence; Maternal Nutrition and the Course of Preg-nancy (Committee on Maternal Nutrition, Food
- and Nutrition Board, National Research Coun-cil, Washington, D.C., 1970), pp. 139-162. R. E. Scammon, in *The Measurement of Man*, J. A. Harris, C. M. Jackson, D. G. Paterson, R. E. Scammon, Eds. (Univ. of Min-nesota Press, Minneapolis, 1930), pp. 173-215. 20. R.
- 21. R. E. Frisch, in Bioscial Internationships in Population Adaptation, E. Watts, F. John-ston, G. Lasker, Eds. (Mouton, The Hague, in press).
- G. C. Kennedy and J. Mitra, J. Physiol. (Lond.) 166, 408 (1963); S. Reichlin, J. B.
- **13 SEPTEMBER 1974**

Martin, M. A. Mitnick, R. L. Boshans, Y. Grimm, J. Ballinger, J. Gordon, J. Malacara, Recent Prog. Horm. Res. 28, 229 (1972). validity of our standards for present-day 23. The middle-class populations is supported by the late A. Damon's recent height and weight data at age 18 years of 522 New England women college freshman: their height and weight are  $165.0 \pm 0.3$  cm and  $57.3 \pm 0.3$  kg, respectively (A. Damon, Soc. Biol. 21, 8 (1974); the mean heights and weights at the same

age of the Frisch-Revelle subjects are 165.6  $\pm$ 0.5 cm and 57.1  $\pm$  0.6 kg, respectively (8)

- A. E. Rakoff, in *The Endocrinology of Human Behavior*, R. P. Michael, Ed. (Oxford Univ. Press, London, 1968), pp. 139–160.
- 25. We thank J. S. Nagel for assistance with the statistical computations and the diagrams, and R. Reed, Harvard School of Public Health, for discussion of statistical methods,

14 May 1974

## **Toxicity in Sponges and Holothurians: A Geographic Pattern**

Abstract. Toxicity in sponges and holothurians is inversely related to latitude and may reach 100 percent for holothurians in high-diversity coral reefs. Evidence from approximately 700 experiments and from underwater observations suggests that predation by fish has resulted in natural selection for noxious and toxic chemical compounds in species within these taxa.

A decade ago it was suggested that toxicity is one of several defense mechanisms that benthic marine invertebrates have evolved in response to predation and grazing by coral reef fish (1). Further information has appeared on toxicity in coral reef benthic invertebrates [see references in (2, 3)]. McAllister (4) stated that only 12 of 770 species of Canadian freshwater and marine fish are toxic to man and most of these are rare. Seven of the 12 toxic species are venomous. In contrast, data from Halstead and Mitchell and from Halstead [cited in (2, 3)], suggested that both venomous and poisonous fish are considerably more common in the tropics than outside the tropics. The data for other marine taxa are insufficient for such a comparison. Because adequate information on toxicity has been unavailable for specific geographic sites, we now report on the extent to which toxicity in sponges and holothurians may change with latitude and with related water temperature and habitat.

Earlier studies (5) indicated that a variety of marine fish are sensitive to steroid saponins (holothurin) from certain holothurians and that, although freshwater fish are slightly more resistant to holothurin, they are suitable as test organisms. Our work has confirmed this. Our experiments were designed to determine if a sponge or holothurian is toxic to fish and to obtain a rough approximation of the degree of toxicity (6). Marine fish were used in many of the studies to ensure that local fish species are responding to toxins from sponges and holothurians with which they are associated. Toxicity in holothurians was tested separately for the body wall, viscera, and Cuvierian tubules. The data presented here are based on extracts from the body wall since this seems to be the most impor-

Table 1. Toxicity of holothurians at various latitudes. For the techniques used by Bakus see (3) and (6). Bakus defines holothurians as highly toxic if the fish dies within 15 minutes (usually less than 10 minutes) and mildly toxic if the fish dies in 20 to 45 minutes. Yamanouchi [see (5) for techniques] used highly toxic if the mean survival time of ten fish (together) was up to 60 minutes and mildly toxic if it was 116 to 173 minutes. Abbreviations: HT, highly toxic; MT, mildly toxic; GJB, Gerald J. Bakus; TY, T. Yamanouchi.

Locality	Lati- tude (°N)	Depth (m)	Number of holothurian species				Investi-
			Tested	Toxic	НТ	MT	gator
San Juan Islands, Washington	48	0–100	12	3 (25%)	0	3	GJB
Onagawa, Japan	38	?	5	4 (80%)	1	3	TY
Seto, Japan	35	?	9	7 (78%)	5	2	TY
Santa Catalina Island, California	33	0–10	2	1 (50%)	0	1	GJB
Guaymas, Mexico	28	0-5	6	5 (83%)	5	0	GJB
Eniwetok, Marshall Islands	12	0–3	4	4 (100%)	4	0	GJB
Palau Islands, Pacific Ocean	7	0–10	11	11 (100%)	9	2	ΤY
Cocos Island, eastern Pacific	6	0-110	7	6 (86%)	6	0	GJB