Europ. J. Cancer, Vol. 16, pp. 519–525

0014-2964/80/0401-0519 $02.00/0

Diet and Menarche in Different Ethnic Groups

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Abstract—*Plasma hormone concentrations have been measured in Bantu girls aged 8–14 yr, who have a late menarche and a low risk of breast cancer, and in Caucasian girls who have an early menarche and are at high risk.*

Plasma dehydroepiandrosterone (DHEA) and the DHEA/androstenedione ratio were significantly higher in Caucasian than in Bantu girls, at all ages studied. LH levels were higher in Bantu girls.

Nutritional factors partially control the age of menarche. Diet-related DHEA levels may be a trigger for the onset of puberty.

INTRODUCTION

SEVERAL epidemiological studies have implicated an early age of menarche in Western societies as a risk factor for breast cancer [1–3]. In view of the long latent period of this disease, MacMahon and his colleagues [4, 5], and others [6] have suggested that a particular endocrine status at puberty, possibly a decreased androgen excretion [7] may be associated with increased risk.

The age of menarche in Western societies differs from that found in African or Asian societies [8, 9] and socio-economic status, rather than ethnic background, is a prime determinant of the initiation of menstruation [10–12].

The steady lowering over the last 50 yr of the age of menarche in successive generations of Japanese [13] and Western [14] girls, and the recent rapid increase in height and weight in Japanese and Japanese–American girls [15] implicate environmental factors, probably diet, as an important feature in earlier maturation.

Despite extensive studies of physiological [16] and endocrine changes [17, 18] in Caucasian girls, the precise nature of the factors initiating puberty are not clear and the endocrine status of girls from late-maturing African or Asian populations has not been reported before.

We have, therefore, studied hormonal status during puberty in South African rural Bantu girls and in North American Caucasian girls.

MATERIALS AND METHODS

Healthy children

Caucasian and Bantu girls, 8–14 years of age, who had not missed more than 10 days of school during the preceding year and who had no overt signs of endocrine abnormality, were selected in New York and in rural areas of South Africa. Age was ascertained by birth certificates or school records; dietary habits were determined by questionnaires completed by the parent or school teacher and by direct observation of school meals or meals fed at home to rural Bantu girls. Informed consent was obtained from parents. The pubic hair and breast development stages were graded according to Tanner [19].

Blood sampling

Peripheral blood samples were taken between 9 and 10 a.m. from the antecubital vein, using 7 ml heparinized vacutainers, from 122 Bantu and 120 Caucasian girls. The plasmas were sent air mail in freezing containers to the American Health Foundation in

Accepted 14 September 1979.

Valhalla, NY, where they were stored at 16°C until analyzed.

Hormone assays

Samples from the same subject were assayed together, while samples from Caucasian and Bantu girls were also assayed simultaneously. All samples were assayed in duplicate.

LH and FSH in the plasma were determined by the method of Midgley [20, 21]. Comparison of the relative potencies of 2nd IRP-hMG, and pituitary standard LER 907 in the immunoassay system was 38 m i.u./μg for FSH and 210 mi.u./μg for LH. The inter-assay and intra-assay variation was 10% and 5% respectively for LH and FSH. LH, FSH and anti-LH and anti-FSH were kindly supplied by NIAMDD, Bethesda.

Prolactin was measured by an homologous RIA using human prolactin hPRL V-L-S-No. 3 and rabbit anti-PRL antibody supplied by NIAMDD [22]. The antibody was used at a final dilution of 1:40,000. Prolactin ^{125}I was purchased from Serona Laboratories, California.

Estradiol and estrone were assayed using cytosol protein binding following separation on Sephadex LH.20 [23].

Androstenedione and dehydroepiandrosterone (DHEA) were measured by RIA [24] after separation on Sephadex LH 20. DHEA was measured by RIA utilizing an antibody raised in rabbits against DHEA-17-oxime BSA; specificity tested against 30 steroids showed only pregnenolone, epiandrosterone, 5α-androsterone-3β-17β diol and testosterone to have a cross reactivity of greater than 0.2%. The latter steroid was eluted prior to DHEA and was not present in the assay.

The sensitivity and recovery of the DHEA is 25 pg/ml and 95%, with an intra and interassay variation of 5% and 10% respectively between 25 and 500 pg/ml DHEA. Sensitivity and recovery for androstenedione was 10 pg and 95% with an intra and interassay variation of 5% and 10% respectively between 10 and 200 pg/ml androstenedione.

Plasma testosterone was measured by radioimmunoassay using dextran charcoal to separate bound from free testosterone [24]. Sensitivity of this assay was 100 pg/ml with an intra and interassay variation of 5%.

Linear regression analysis and statistical analysis using Student's *t*-test were performed to determine the inter-relation of hormone levels and to determine hormone difference between different groups of girls.

RESULTS

DHEA

Caucasian girls showed significantly higher DHEA levels than Bantu girls at all ages from 9 to 14 (Fig. 1). The levels increased during the pubertal period in both groups, but to a somewhat greater extent in Caucasians, so that the difference was even greater at age 14 than at age 9.

Androstenedione

In contrast to DHEA, levels of androstenedione were significantly higher in Bantu than in Caucasian girls at ages 9, 10 and 13 (Fig. 1). Levels increased during puberty in both groups, and once again to a greater extent in Caucasians, so that there was no longer a significant difference between Bantu and Caucasians by age 14.

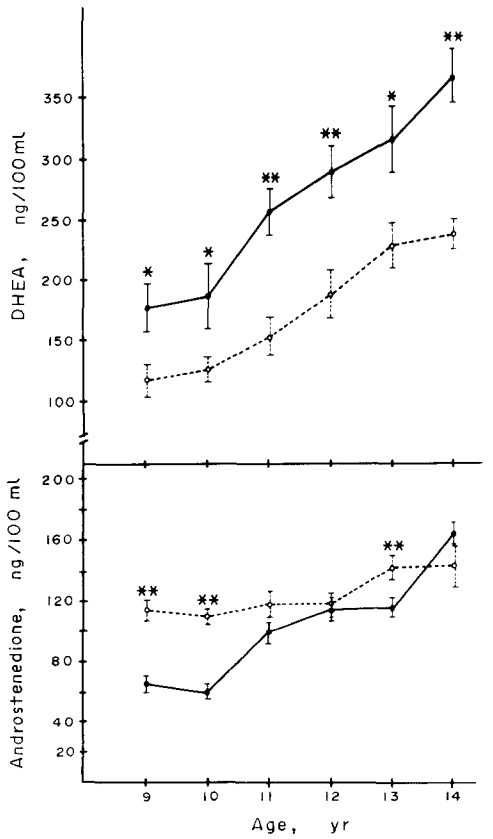

*Fig. 1. Plasma DHEA and androstenedione during puberty in Bantu (○—○) and Caucasian (●—●) girls. A minimum of 16 girls per group. Results given as mean ± S.E. *$P \leqq 0.05$ **$P \leqq 0.01$.*

Table 1. *Plasma estradiol, estrone, testosterone, LH, FSH and prolactin in Caucasian and Bantu girls from* 8–14 yr *of age*

		Age (years)	Pubertal stage	Estradiol (ng/100 ml)	Estrone (ng/100 ml)	Testosterone (ng/100 mg)	LH (μg LER 907)	FSH (per 100 ml)	Prolactin (ng/ml)
Caucasian	(17)*	9	B_1PH_1	7.1±0.5†	20.5±2.1	19.5±1.0	2.3±0.1	11.6±1.0	8.6±1.0
Bantu	(20)	9	B_1PH_1	7.0±0.4	26.7±1.2	21.0±1.5	4.5±0.1‡	15.0±1.1§	9.2±0.5
Caucasian	(20)	10		6.2±0.3	23.8±1.9	22.3±1.8	3.4±0.1	17.5±1.6	8.3±1.0
Bantu	(19)	10		6.7±0.4	28.6±1.5	24.8±1.9	4.5±0.3‡	19.1±1.8	9.0±0.8
Caucasian	(19)	11		7.0±0.4	22.2±2.5	27.3±2.7	3.8±0.2	17.9±1.6	9.7±0.9
Bantu	(20)	11		8.7±0.6	26.4±1.4	29.6±1.9	4.9±0.2‡	20.0±2.1	9.0±0.9
Caucasian	(19)	12		7.7±0.6	27.4±2.0	32.5±2.6	4.4±0.2	16.6±1.5	8.5±0.8
Bantu	(16)	12		7.6±0.4	27.5±1.8	36.1±2.8	5.0±0.3	19.9±1.5	7.4±0.7
Caucasian	(21)	13		10.7±0.5	29.5±1.3	29.8±1.7	4.6±0.3	17.7±1.4	8.3±1.3
Bantu	(20)	13		11.8±0.5	26.1±1.4	37.5±2.5	5.8±0.3§	24.0±1.5‡	9.2±0.8
Caucasian	(21)	14	B_4PH_4	10.7±0.5	32.2±1.0	28.6±1.6	5.1±0.3	20.1±1.0	10.6±0.6
Bantu	(17)	14	B_4PH_4	12.5±0.7	30.1±0.7	40.5±3.3	6.6±0.9	26.2±2.3‡	9.5±0.8

*Number per group.
†Results given as mean±S.E.
‡$P \leqslant 0.01$—Bantu vs Caucasian girls.
§$P \leqslant 0.05$—Bantu vs. Caucasian girls.

DHEA/androstenedione ratio

At age 9, the DHEA/androstenedione ratio was nearly 3.0 in Caucasian girls, but only about 1.0 in Bantu girls. By age 14, the ratio had declined slightly, to about 2.0 in Caucasians and had risen slightly to about 1.25 in the Bantu.

LH

LH levels increased slowly and progressively from 9 to 14 years of age in the Caucasian girls (Fig. 1). In Bantu girls, the rise started at age 10 and then continued progressively to age 14. The values in the Bantu were significantly higher than those in Caucasian girls.

LH and DHEA

A linear correlation between plasma levels of LH and DHEA were present in Caucasian but not Bantu girls with increase in age (Fig. 2).

FSH

The rise in FSH levels during puberty was not quite so smooth as in the case of LH (Table 1). Caucasian girls showed a rise from age 9 to 10, a plateau from age 10 to 13, and another rise from age 13 to 14. Bantu girls showed a rise from age 9 to 10, a plateau from age 10 to 12, and then a progressive increase between age 12 and age 14. The values were slightly higher in Bantu than in Caucasian girls at all ages between 9 and 14.

Testosterone

Plasma testosterone levels rose slightly from age 9 to age 11 in Caucasian girls and essentially plateaued thereafter from age 11 to age 14 (Table 1). The levels rose progressively between ages 9 and 14 in Bantu girls. Values were higher in Bantu at all ages; the difference was very slight at age 9 but increased progressively, reaching about 50% at age 14 ($P<0.01$).

Estradiol

The differences between groups and between ages were small and inconsistent (Table 1).

Estrone

Levels were approximately constant from age 9 to age 14 in Bantu girls. In Caucasian girls, they were about 80% of Bantu values at age 9 and rose gradually to equal Bantu values at age 12 and thereafter.

Prolactin

Plasma prolactin, which was comparable in both groups of girls did not change significantly between 9 and 14 years of age (Table 1).

DISCUSSION

The most striking hormonal differences between the rural Bantu and the urban Caucasian girls were higher plasma DHEA concentrations, the higher DHEA/androstenedione ratio, and the lower LH concentrations in Caucasian girls during puberty.

There is evidence to suggest that initiation of puberty is related to a gonadostatic threshold [25], but several studies of healthy children [26, 27] indicate that early adrenal

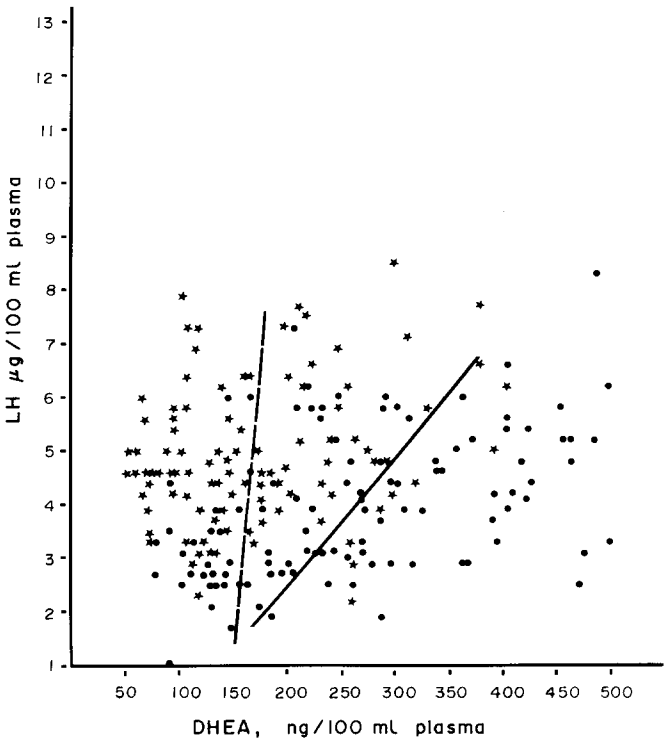

Fig. 2. Plasma LH and DHEA levels in Caucasian (●) and Bantu (★) girls, 8 to 14 yr of age. Caucasian girls, LH:DHEA show a linear correlation (—; $r=0.501$, $P\leqslant 0.01$, $F=31.4$, $n=117$) while no correlation is evident in Bantu girls (- - -; $r=0.265$, $P\leqslant 0.05$, $F=7.45$, $n=112$).

Table 2. Age of menarche, height, weight and dietary composition of Bantu and Caucasian girls

	Bantu	Caucasians
Age of menarche (yr)	14.9	12.6
Height (cm at 14 yr)	150±7*	161±7.5
Weight (kg at 14 yr)	40±6*	52±8
Total calorie intake daily	1580†	2060
%Calories as:		
Carbohydrates	72%	52%
Fat	16.5%	35%
Animal protein	3.6%	7.0%
Vegetable protein	7.0%	4.5%

*Height range—147.7±7.1 to 152±7.3 cm and weights 38.9±8 to 42.6±6.7 kg for Bantu girls depending on the rural location (37) giving a mean surface area between 126 to 134 for girls 14 years of age, estimated from normographs after duBois and duBois [48].

†Louw *et al.* [36].

maturation may play a part in the maturation of the hypothalamic–pituitary axis. In experimental animals, administration of DHEA leads to an increase in plasma LH levels [28]. Aromatization of androgens of adrenal origin may occur in the hypothalamus in animals [29], leading to a feedback on LH secretion, but whether this happens in man is unknown. In this study, the increase in plasma LH was correlated with an increase in DHEA in Caucasian ($R=0.50$, $P<0.01$) but not in Bantu ($R=0.26$, $P<0.05$) girls. Although Collu and Ducharme [30] have reported a correlation between the increase of LH and androstenedione, no relationship was evident in this study.

During puberty, changes in the amplitude of LH release [31] and development of a two phase release of LH [32] occur. The relationship of increasing DHEA and/or androstenedione levels to changes in LH activity remain to be clarified.

Turning from the role of androgens in the initiation of puberty to the effects of environmental factors on endocrine status, it is quite clear that adrenal activity is altered by calorie intake [33–35]. The rural Bantu in our study were smaller and lighter at 14 years of age than Caucasian girls. The former eat a diet of a few staple foods, mainly vegetables and fruit [36], which supplies about 25% less calories per day than that obtained by Caucasian children of comparable age [37] (see Table 2). Thus, the lower plasma DHEA levels in Bantu girls is very probably related to their lower calorie intake. If 3β-hydroxysteroid dehydrogenase activity were less active in Caucasian girls or if there were differences in the clearance rate of DHEA, this would explain the higher androstenedione and testosterone levels in Bantu girls.

With regard to physiological and endocrine development, Burgess and Burgess [38] have reported that Ugandan girls reach a peak height velocity growth 6 months before British girls, although they reach menarche 3 months later. Richardson and Pieters [39] state that Bantu girls who had not reported a mense by 14 years of age, were sexually well-developed (Stage B3–B4, PH 2–3). Thus, these girls had failed to menstruate in spite of being past the criteria for menstruation to have taken place. In our study, all the 14-year old Caucasian girls had experienced several menses but the majority of the Bantu girls had not menstruated despite the fact that they were sexually well-developed.

In this regard, the importance of body build and type as a determinant in the timing of menarche has been previously reported [40–42].

In a study of urban Bantu girls in Durban, Kark [43] separated 14-year-old girls into pubescent, those who had not attained menarche, and adolescent, those who had attained menarche. Pubescent girls had a body weight 43.4 ± 6.2 kg and height 149.2 ± 5.4 cm, while adolescent girls had a body weight 49.7 ± 6.0 kg and height 153.5 ± 6.2 cm. Thus, pubescent and adolescent girls had body surfaces of 1.33 and 1.43, respectively, menarche occurring within this range. Thus, the mean body surface of white girls was 1.53, all having attained menarche, while the mean body surface for Bantu girls aged 14 years is 1.32. Since body surface can be associated with onset of menarche, attainment of a critical level of DHEA may be necessary to produce LH surges, as suggested by Kraulis *et al.* [44] and, therefore, the onset of menarche.

The failure to menstruate in the Bantu girls would appear to be comparable to dietary amenorrhea, evident in many underweight Caucasian girls [45], and to the lack of cyclic activity in some underweight girls and women [46]. Several studies indicate a direct relationship between inadequate nutrition and the delayed occurrence of menarche and menstrual cycles [47, 48]. Earlier menarche in well-nourished 'well-to-do' Bantu [8], Japanese, or Latin American girls [15] supports the conclusion that the initiation of menarche is affected by nutrition.

We postulate that failure to menstruate at an appropriate sexual maturity, and failure to establish regular menstrual cycles are related to the same factors—namely, delayed adrenal maturation and a delay in reaching the critical weight to body fat ratio necessary to initiate menses, and that these are the factors that confer subsequent protection against breast cancer.

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