action on epidermal cell membranes or is indirectly evoked by the invading inflammatory cells. Some of the arachidonic acid cascade metabolites have chemotactic activities and others, including PGE_1, may modulate the chemotactic response (13). The increased PGE_1 formation by epidermal tissue might be an essential contribution to the development and persistence of primary irritant dermatitis. Therapeutic attempts to regulate PG formation in inflammatory skin conditions such as primary irritant dermatitis should therefore be made to control epidermal PG synthesis.

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Androgen Abnormalities in Acne Vulgaris

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Abstract. Thirty-six women with acne vulgaris who consulted gynecologist with complaints of hirsutism, infertility, menorrhagia, or oligomenorrhea were evaluated for an androgen abnormality with assays for testosterone (T), androstenedione (A), and dehydro-epi-androsterone (DHEA). Forty-eight percent of the DHEA measurements were elevated and 61% of the patients had elevation of one or more of the three measurements. The frequency of abnormal androgen levels remained relatively constant regardless of the severity of the presenting signs and symptoms. This study calls attention to the high frequency of an androgen abnormality in acne patients who also have evidence of hirsutism, menstrual irregularity, and/or infertility. Consideration should be given to assaying DHEA, T, and A levels in an effort to discover those patients who have a systemic endocrine disorder, of which acne manifests as a sign.

Key words: Acne; Androgens; Hirsutism; Infertility; Oligomenorrhea

Acne vulgaris, the multifactoral dermatologic disorder of the pilosebaceous apparatus, is a common entity frequently affecting adolescents and young adults. Androgenic stimulation of the sebaceous glands has been implicated as a major etiological factor in the pathogenesis of the entity (3).

It has been shown that sebum production by the sebaceous gland is stimulated by androgens, primarily testosterone and its metabolite dihydrotestosterone (DHT) (1). Some studies have implied that excessive levels of androgens in the skin are contributory to the lesions of acne, as androgens stimulate the mitotic activity in the sebaceous glands, fibroblasts, and hair follicles, resulting in obstruction of the pilosebaceous unit (7).

Research reported in 1974 stated that in females, plasma testosterone levels were significantly elevated in patients with acne (2). A contradicting report, in 1975, stated that plasma testosterone levels are normal in most acne patients (10).

Another report showed increased levels of DHEA sulphate in females afflicted with acne, in comparison with age-matched controls (11). This is probably an inactive androgen and thus its significance is not clear.

Most interesting is a 1978 study of acne therapy with estrogen and the androgen blocker, cyproterone acetate (5). Of the 20 patients used in that study, 8 (40%) had an elevation in their baseline plasma testosterone levels. The authors noted a significant fall in plasma testosterone level during successful therapy in these patients.

Despite numerous reports, no truly conclusive evidence has been presented to show that patients with acne have abnormal circulating levels of serum androgens (4, 6). The purpose of the present study was to fully document serum androgen profiles in 36 female patients who consulted their gynecologist with complaints of hirsutism, infertility, menorrhagia, or oligomenorrhea and on physical examination had evidence of acne vulgaris. It is to be noted that this population represents only a small subsection of the acne patients seen by the dermatologist and the information reported in this paper may only be applied with certainty to that subsection.

MATERIAL AND METHOD

All patients initially consulted a gynecologist's office with complaints of infertility, oligomenorrhea, menorrhagia, or hirsutism. None of the patients had acne as a chief complaint. Facial acne was found on physical examination of the patients reported in this paper. The acne was given a designation "mild" if 20 or fewer inflammatory papules were present on the face and there was no evidence of nodulocystic acne. The designation "moderate" was applied to patients having more than 20 inflammatory papules and small areas of nodulocystic acne. No patients were found to have "severe" acne, which would have implied extensive nodulocystic disease. The designations were made at the initial office visit by the same observer.

The patients who were also facially hirsute were designated as 1+ to 4+ hirsute. Patients designated as "1+" hirsute had scattered terminal chin hairs. Patients designated as "2+" had clumps of terminal chin hairs. Patients designated as "3+" hirsute had either chin and anterior neck covered with terminal hairs. One "4+" hirsute female had full male beard growth and distribution, including chin, anterior neck, and cheek areas.

The serum levels of testosterone (T), androstenedione (A), and dehydro-epi-androsterone (DHEA) were all measured by radioimmunoassay after informed consent was obtained.

RESULTS

The results of the hormonal assays of testosterone, androstenedione, and dihydro-epi-androsterone are presented in Table I for each patient, along with the patient's age, menstrual history, and acne and hair evaluation. It should be noted that 11 patients are absent from one of the three assays and a 12th patient's age, menstrual history, and acne and hair due to laboratory error.

It was found that the average DHEA level in these patients was 802 ng/dl, with normal being less than 700 ng/dl. Even with the elimination of the highest value (patient no. 30, whose value was almost twice that of the next highest level) the overall average is still greater than normal, at 722 ng/dl. Of the 33 patients assayed, 16 (48%) had assays elevated above the normal range.

The serum testosterone levels were elevated in only 6 of the patients (range 24–128 ng/dl, normal less than 90, mean 64). Androstenedione levels were elevated in 3 of the patients assayed, with an average of 184 ng/dl and range of 42–342 (normal <300).

In these 36 patients with acne on examination, who consulted mainly for a gynecological complaint, 22 (61%) had at least one abnormally elevated androgen value recorded. Twenty-six patients had DHEA and T levels recorded, and 15 (58%) had at least one elevation. Finally, of the 33 patients with DHEA levels recorded, 16 (48%) were elevated.

By examining Table I it will be seen that a significant number of patients with acne had elevated androgen levels regardless of presenting symptomatology. More than 50% of patients had DHEA elevations in the groups with regular menstruation, with oligomenorrhea, without hirsutism, and with 3+-4+ hirsutism and with only mild acne. The percentage of patients with elevated testosterone and androstenedione levels remained relatively constant and compatible with the overall group in all subgroups.

DISCUSSION

The data presented demonstrate the presence of abnormal elevations of serum androgens—particu-

Table 1. *Serum androgen studies in acne patients*

Normal values: T = less than or equal to 90 ng/dl, A = less than or equal to 300 ng/dl, DHEA = less than or equal to 700 ng/dl. T = testosterone; A = androstenedione; DHEA = dehydro-epi-androsterone; R = regular; A = amenorrhea; O = oligomenorrhea

Pat.	Age	Menses	Hair	Acne	T	A	DHEA
1	29	R	2+	Mod.	96	120	490
2	26	R	3+	Mild	123	160	1 270
3	18	O	O	Mod.	92	80	637
4	14	R	0	Mild	–	90	470
5	20	R	3+	Mild	–	260	1 200
6	24	O	0	Mild	82	200	730
7	30	O	2+	Mild	76	340	498
8	18	O	0	Mild	–	220	1 044
9	17	A	0	Mild	29	270	610
10	18	A	0	Mild	–	140	960
11	20	O	3+	Mild	–	–	750
12	30	R	0	Mild	75	–	845
13	18	R	1+	Mod.	128	–	644
14	27	R	0	Mod.	44	120	340
15	18	R	3+	Mild	55	270	1 040
16	26	O	3+	Mild	56	122	690
17	22	O	0	Mild	91	160	1 110
18	34	R	3+	Mild	24	127	670
19	28	R	1+	Mod.	41	291	1 220
20	14	O	0	Mod.	–	160	760
21	23	O	3+	Mild	71	324	290
22	32	R	2+	Mild	31	174	1 710
23	14	O	0	Mild	55	237	950
24	23	O	2+	Mild	51	225	640
25	21	R	0	Mod.	81	342	850
26	27	A	1+	Mild	41	145	550
27	26	R	0	Mod.	34	42	–
28	20	O	4+	Mild	64	209	340
29	25	O	2+	Mild	48	150	–
30	29	O	4+	Mild	47	158	3 350
31	29	A	0	Mild	124	256	350
32	28	O	2+	Mod.	–	95	190
33	24	R	2+	Mild	31	112	200
34	14	R	0	Mod.	63	193	420
35	25	A	0	Mild	30	195	150
36	29	O	2+	Mild	74	137	–
Mean	23				64	186	802
S.E.M. ±					5.5	13.4	100

larly DHEA—in this group of female patients with acne vulgaris. Elevation of either testosterone, androstenedione, or DHEA occurred in approximately 60% of these patients, with a DHEA elevation found in almost half of the patients studied.

The elevated androgen levels strongly imply that, in this series of patients with hirsutism, infertility, menorrhagia, or oligomenorrhea, systemic disease should be considered together with the dermatologic manifestation of acne as being a sign rather than an independent disease entity. It has been reported that in this setting, partial hydroxylase deficiencies are often the underlying systemic disorder (8) and may necessitate a different pharmacologic therapy (9) than if the acne existed isolated from other systemic abnormalities.

From this study it is clear that acne may be a manifestation of a generalized endocrinological disorder in the female. Specific enquiry regarding earlier menstrual irregularities and/or infertility, and careful noting of signs of hirsutism on physical examination appear to be a reliable way of determining which acne patients are at increased risk. It appears from our data that any acne patient with any sign or symptom of menstrual or fertility disorder, or hirsutism, regardless of severity, should have a DHEA assay performed in an effort to discover those patients who might have an underlying

generalized endocrine disorder. From our study, DHEA is clearly the single most sensitive hormonal assay in this regard, while the addition of testosterone and androstenedione measurements does increase the discovery of patients with abnormally androgen levels. These patients with androgen abnormalities deserve thorough endocrinologic evaluation in an effort to treat both the acne and the endocrinological disorder.

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Spontaneous Cell-mediated Cytotoxicity (SCMC) in Patients with Alopecia Universalis

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Abstract. The spontaneous cell-mediated cytotoxicity (SCMC) of unfractionated lymphocytes was determined in 5 patients with alopecia universalis (AU). The target cells used were K562 and Chang cell lines. All patients had an increased SCMC as compared with age- and sex-matched donors. The results indicate that SCMC against K562 cells is more pronounced than that against Chang cells.

Human lymphocytes are known to express at least four kinds of cytotoxicity:

1. Cytotoxic activity of T lymphocytes previously sensitized against the target cells.

2. Cytotoxicity exerted by lymphocytes in the presence of humoral antibodies directed against relevant antigens on the target cells (antibody dependent cell-mediated cytotoxicity = ADCC).

3. Spontaneous cell-mediated cytotoxicity (SCMC) with no known presensitization history against the target cells, performed without addition of external antibodies. The lymphoid cells mediating this spontaneous or natural cell-mediated cytotoxicity have been termed natural killer (NK) cells.

4. Cytotoxicity induced by mitogens such as phytohemagglutinin (PHA) or concanavalin-A (Con-A). Lymphocytes activated by PHA or Con-A lyse target cells of allogeneic and syngeneic origin.

In our previous studies we found that the ADCC of non-fractionated lymphocytes was higher in patients with both alopecia areata (AA) and alopecia universalis than in normal controls (4). In the present study we looked for spontaneous cell-mediated cytotoxicity (SCMC) in patients with alopecia universalis.

MATERIALS AND METHODS

Patients and controls

Five patients with AU from our earlier study (4) were examined (Table I). The normal controls were matched according to age and sex.