

## Stress, Acne and Skin Surface Free Fatty Acids

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**Emotional stress was accompanied by an exacerbation of acne vulgaris lesions and an increase in skin surface free fatty acids (ffa). Surface total lipids did not show a statistically significant change during the period of stress. A cause-and-effect relationship has not been established between skin surface free fatty acids and acne vulgaris, but this and other indirect evidence suggest that ffa may play an important role in the pathophysiology of acne.**

Several authorities reflect the commonly held clinical impression that emotional stress exacerbates acne vulgaris (1, 2). Laboratory support for this observation, utilizing newer methods of lipid quantitation and evaluating a group of subjects large enough for statistical analysis, is not available. Therefore, the purpose of this study was to investigate the effect of one form of emotional stress on acne, by evaluating and coordinating the development of clinical acne lesions with changes in skin surface total lipids and skin surface free fatty acids (ffa). These two aspects of skin surface lipids were studied because evidence suggests that they are important in the pathogenesis of acne. For example, individuals with acne are more likely to have higher values for skin surface total lipid production than do individuals without acne (3). Concerning the ffa, it was recently shown that improvement of acne with sys-

temic tetracycline parallels a drop in surface ffa (4). These fatty acids are the most irritative component of skin surface lipids and intracutaneous injection of small amounts of ffa, as compared to other surface lipids, produces a marked inflammatory response (5).

### MATERIALS AND METHODS

Eight male and 1 female, first-year Case Western Reserve University medical students with a history of acne were studied. A compulsory 8-hr academic examination covering 10 weeks of study was used as the stressful situation. Skin surface lipids were collected before, during and after the examination period. Western Reserve students receive one examination every 10-12 weeks and are not under constant stress from frequent testing.

One student had been taking vitamin A for acne. This was stopped 2 weeks before the start of the study. No other systemic acne therapy was used prior to nor at any time during the study. No local acne therapy was used for 1 week prior to collections. The students, who washed with Ivory soap throughout the study, were instructed not to use cosmetic preparations containing antibacterial substances.

Both total lipid and ffa collections were made on 2 consecutive days 3 weeks before the examination, 2 days before the examination, 2 days before and 2 weeks after the results were published. On collection days, the students washed their faces in the morning and collections were made at the same time each evening for each subject.

The technic for collecting skin surface total lipids

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was adapted from the procedure used by Kirk and Chieffi (6). A 36.4 sq cm area on the cheek was washed three times with 20 ml reagent grade acetone introduced into a glass cylinder held against the skin. The boundary of the washed area was delineated with a marker containing a lipophilic dye. This marker allowed the observer to visually detect the migration of surface lipids into the cleaned area. Three hours later, the central 27.4 sq cm of the larger area was examined for evidence of this migration; if free of such lipids, the area was washed three times with 15 ml reagent grade acetone. These latter washings were filtered through lipid-free paper, evaporated into micro weighing bottles, desiccated over  $\text{CaCl}_2$  and olive oil, and then weighed to constant weight. The ability of acetone washings to remove surface lipids was shown when lipid removed by three additional acetone washings of the 27.4 sq cm area was consistently less than 3% of that removed by the first three washings.

The technic for collecting and measuring ffa has been outlined in detail (7). A 14.5 sq cm area on the forehead was washed three times with spectro-quality acetone introduced into a glass cylinder held against the skin. The boundary was outlined with the dye marker and the same precautions taken to exclude lipid migration. Three hours later, the central 5.2 sq cm area was washed twice with 3 ml of an acidified heptane-isopropyl alcohol mixture. These latter washings were combined and water soluble acids removed by aqueous extractions. The residual acids were measured by a nonaqueous titration system using tetrabutylammonium hydroxide as the titrant. The effectiveness of the heptane-isopropanol mixture in removing surface ffa was determined by applying 0.5  $\mu\text{Eq}$  oleate- $1\text{-}^{14}\text{C}$  to the skin and then determining the radioactivity in the heptane-isopropanol mixture used to wash the area of oleate- $1\text{-}^{14}\text{C}$  application. By comparing this radioactivity to that of 0.5  $\mu\text{Eq}$  pure oleate- $1\text{-}^{14}\text{C}$ , the amount of ffa recovered was found to be 93 and 94% in 2 subjects studied.

Surface ffa collections were done in 7 subjects. Inability to seal the collection cylinder tightly against the forehead prevented ffa collections in the other 2 subjects.

The study was designed to fit Rothman's suggestion: if the influence of any factor on excretion of fatty acids is to be examined, tests should be done on the same individual or the same group of individuals in pre-experimental and experimental conditions (8). The students acted as their own controls. In an attempt to minimize any effect the

environment (temperature, humidity, wind, etc) might have on skin surface lipids, there were control periods both before and after the period of stress. Controls for each subject were values obtained from two collections 3 weeks before the exam and two collections 2 weeks after test results were announced. Stress values were those obtained from collections immediately before the examination and before examination results were announced. Each subject, therefore, had four control values for skin surface total lipid production and skin surface ffa production, and four stress values for the same measure of surface lipids.

Acne lesions were clinically evaluated by counting the number of pustules in a  $6 \times 6$  cm area on both cheeks. Comedones and papules were not enumerated and cystic lesions were not encountered during the course of this study. The control value for each subject was the mean number of pustules present 3 weeks before the examination and 2 weeks after the results were announced. Stress values were the means of the number of pustules present immediately before the examination and before the results were announced.

## RESULTS

Table 1 presents the mean and standard deviation of each subject's four control and four stress values for skin surface total lipid and skin surface ffa production. Table 2 summarizes surface total lipid data; here changes are expressed as percentage increase or decrease of stress values from control values. Table 3 summarizes ffa data in a similar manner.

An analysis of variance was used for statistical evaluation of data. A significant increase in skin surface ffa production was observed during the period of stress ( $p < 0.005$ ). No significant change in surface total lipid production was observed during the same period ( $p > 0.1$ ). At the time this study was conducted, another experiment measuring the same parameters of surface lipids was being done in a group of normal adult men. The control group in this latter study received nothing known to alter surface lipids. Their surface lipid values were

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**Table 1. Mean Control and Stress Values for Skin Surface Total Lipid Production and Skin Surface Free Fatty Acid Production**

Subject	Values	Total lipid (mg/27.4 sq cm/3 hr)	Free fatty acid ( $\mu$ Eq/6.2 sq cm/3 hr)
		Mean (SD)	Mean (SD)
1	C	8.4 $\pm$ 0.7	.547 $\pm$ .080
	S	7.2 $\pm$ 0.3	.627 $\pm$ .101
2	C	3.9 $\pm$ 0.4	
	S	4.0 $\pm$ 0.3	
3	C	3.8 $\pm$ 0.2	.282 $\pm$ .057
	S	3.6 $\pm$ 0.5	.335 $\pm$ .037
4	C	4.2 $\pm$ 0.7	.735 $\pm$ .148
	S	4.6 $\pm$ 0.5	.911 $\pm$ .154
5	C	3.4 $\pm$ 0.3	.136 $\pm$ .025
	S	3.0 $\pm$ 0.3	.179 $\pm$ .036
6	C	3.2 $\pm$ 0.4	
	S	2.9 $\pm$ 0.1	
7	C	6.9 $\pm$ 0.4	.223 $\pm$ .055
	S	6.0 $\pm$ 0.1	.318 $\pm$ .108
8	C	5.4 $\pm$ 0.3	.708 $\pm$ .179
	S	5.4 $\pm$ 0.2	.857 $\pm$ .200
9	C	1.4 $\pm$ 0.4	.069 $\pm$ .034
	S	1.5 $\pm$ 0.3	.082 $\pm$ .037

C, control; S, stress.

**Table 2. Effect of Stress on Total Skin Surface Lipid Production**

Production change	No. of subjects	Average change (% of control values)	Range (%)
Increase	3	6	4-8
Decrease	5	11	5-14
Unchanged	1	—	—

**Table 3. Effects of Stress on Skin Surface ffa Production**

Production change	No. of subjects	Average change (%)	Range (%)
Increase	7	22	19-42
Decrease	0	—	—

organized according to the same time intervals as the stress and control periods of the student experiments. No significant change in either surface ffa or surface total lipids occurred during the time surface ffa rose in the medical students.

Three of the 9 students had pustules during the control period of the study. These 3 had an increase in number of pustules during the period of stress. Of the 6 students free of pustules during the control period, 5 developed several pustules during the stressful period. The increase in these acne lesions was statistically significant ( $p < 0.01$ , Sign Test). Since this study did not follow other acne lesions, no conclusions can be drawn concerning the effect of stress on comedones and papules.

An incidental finding was the considerable variability of total lipid and ffa values from 1 subject to another. An analysis of variance showed this variation among individuals to be highly significant ( $p < 0.0005$  for both ffa and total lipid).

**DISCUSSION**

Academic examinations have been used in previous studies on the biologic effects of stress (9, 10, 11); stressfulness of examinations is well documented in the psychiatric literature (12). The study reported in this paper showed such an examination was associated with increase in skin surface ffa and exacerbation of acne. Although a cause-and-effect relationship was not established, this and other indirect evidence suggest that these ffa may play a major role in acne pathogenesis. For instance, others have reported improvement of acne with systemic tetracycline which parallels a fall in skin surface ffa (4).

The way in which ffa may exacerbate acne is unknown, but it is known that ffa are the most irritating component of skin

surface lipids; intradermal injection of these acids produces a marked inflammatory response (5). A similar phenomenon may exist in acne when rupture of the sebaceous follicle release lipids into the dermis. These follicular lipids contain ffa and possibly the greater the amount of ffa, the greater the inflammatory response.

The mechanism by which emotional stress is related to rise in skin surface ffa was not studied and cannot be determined from our data. Possible explanations may be related to other stress-induced biologic alterations such as changes in systemic lipid metabolism, changes in bacterial flora of the skin or changes in adrenal function.

Systemic lipid alterations with stress include elevation of plasma ffa (9). This rise in plasma ffa is inhibited by ganglionic blocking agents, so it is likely that increased activity of the autonomic nervous system is involved. The relation of plasma ffa changes to skin surface ffa changes is not known.

Emotional stress is associated with increased sweating. Profuse sweating, which interferes with the self-sterilizing power of normal skin (13), is accompanied by a transient rise in bacterial flora of normal skin (14). Such a rise could account for increase in surface ffa since bacterial lipase activity plays a role in formation of ffa from sebum triglycerides (15). The importance of increased bacterial flora in the increase in ffa observed in this study is difficult to ascertain since no attempts were made to evaluate changes in our subjects' skin flora.

With stress, adrenal corticosteroids are released in increasing amounts and steroid acne is a well recognized entity; however, the role of corticosteroids is unknown in ffa changes in our report.

Statistical analysis of changes in skin

surface total lipid did not show a significant change during the time of stress. This finding does not necessarily contradict the data published by Wolff et al (16) and Pochi et al (17). The former reported 3 subjects in whom an increase of facial sebum occurred during acute periods of stress. One of these subjects demonstrated a correlation between the number of acne pustules and periods of mood alteration. The technic employed by Wolff et al for sebum quantitation was adapted from that developed by Jones et al (18). This method attempts to measure sebum by the degree to which it displaces a hydrocarbon film on a watery surface. Further evaluation of this procedure revealed that displacement of the hydrocarbon film was not a function of total sebum, but was directly related to the total amount of ffa in the sebum (19). Total sebum values could be extrapolated from hydrocarbon film displacement only if the ffa content of sebum were constant; it has recently been shown that there is considerable variability in the ffa concentration of sebum (20). The data of Wolff et al therefore showed increase in skin surface ffa during emotional stress rather than increase in total sebum. Such an interpretation of their data makes their results consistent with the findings reported in this study.

Pochi et al (17) found that a woman's sebum production increased after the death of her mother. In addition to increased surface lipids, they detected an increase in urinary 17-ketosteroids. The stress was felt to have increased production of adrenal corticosteroids including androgenic compounds; these in turn stimulated the sebaceous glands to produce more surface lipids. Others have documented the increase in urinary 17-ketosteroids with stress (21), and it is known that adult female

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sebaceous glands will respond to increase in androgen activity (22).

Failure of this study to demonstrate a significant alteration in surface total lipids does not necessarily contradict the finding of Pochi et al. An important difference exists between our group of students and the patient they report; their study was done on a woman and, of the 9 students in our study, 8 were men. Such a difference in sex distribution may be important, since the normal degree of androgenic stimulation for sebaceous glands to produce surface lipids is different for the two sexes. Adult male sebaceous glands are normally under maximal stimulation by androgens (22). Skin surface lipid production of men will therefore not respond to extra androgens; in this way, surface lipid production in adult males differs from that in adult females. If increased adrenal androgen was the stimulus for increased surface lipids in the woman studied by Pochi et al, the same stimulus would not be expected to increase surface lipids in the men reported in this study. Although it is an isolated observation, the 1 female student in this study did show increase in surface total lipid production during the period of stress.

### SUMMARY

A prospective study was initiated to evaluate the commonly held clinical impression that emotional stress can exacerbate acne vulgaris. The number of experimental subjects participating in the project facilitated a statistical evaluation of observations made during the study. Emotional stress, provided by an academic examination, was accompanied by increase in number of acne lesions ( $p < 0.01$ ). The stressful experience and acne exacerbation were associated with increase in skin surface free fatty acid production ( $p < 0.005$ ). Al-

though this study does not establish a cause-and-effect relationship between acne and skin surface free fatty acids, it adds to other indirect evidence which suggests that these fatty acids may play a role in the pathogenesis of acne.

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