Changes in skin surface lipid composition induced by severe caloric restriction in man[1,2]

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Lipid collected from the surface of the human forehead is predominantly (~95%) the product of the sebaceous glands (1) and contains on the average 41% triglycerides, 16.5% free fatty acids, 25% wax esters, 12% squalene, 1.5% cholesterol, 2% cholesterol esters, and 2% diglycerides (2). This sebum composition shows little variation between normal subjects or over long periods of time in individual subjects, except for the degree of hydrolysis of triglycerides to free fatty acids effected by bacteria (3). We reported previously, however, that the proportion of squalene in this mixture increases markedly in obese subjects undergoing prolonged total fast for weight reduction (4). This change resulted from suppression of the synthesis of all sebum constituents other than squalene, the production of which remained essentially constant. We now have evidence that a similar change in the composition of sebum occurs in normal nonobese subjects under essentially fasting conditions.

Material and methods

Volunteer subjects consisted of three women and one man, who were at most only moderately in excess of optimal weight. During a 10-day fasting period they were permitted two cups of beef bouillon per day, water ad libitum, and a vitamin mixture supplement for a total daily intake of fewer than 50 kcal. Surface lipid was sampled from the forehead at the same time each day during a preliminary 1-week period, the fasting period, and for at least 10 days after resumption of a normal diet. The lipid samples were collected by rubbing the forehead skin area with a small, hexane-soaked polyurethane sponge mounted on a wire handle and recovered by extraction of the sponge with hexane. The extracts were evaporated under nitrogen and stored at −20 C until analyzed.

Ten-microgram aliquots of the lipid samples were analyzed by a quantitative thin-layer chromatographic procedure developed for this purpose (5).

Results

After 5 to 7 days of fasting, the forehead surface lipid of all four subjects showed a marked increase in the proportion of squalene, which continued to rise until the end of the fast and then declined several days after normal diet was resumed. In view of the similarity of the subjects' response, the average lipid composition of the four subjects on each day of the experiment was calculated and is shown in Fig. 1; the values for triglycerides, diglycerides, and free fatty acids are combined to minimize variability due to bacterial hydrolysis of the sebum.

Discussion

The delay in appearance of the changed sebum and the degree of change observed

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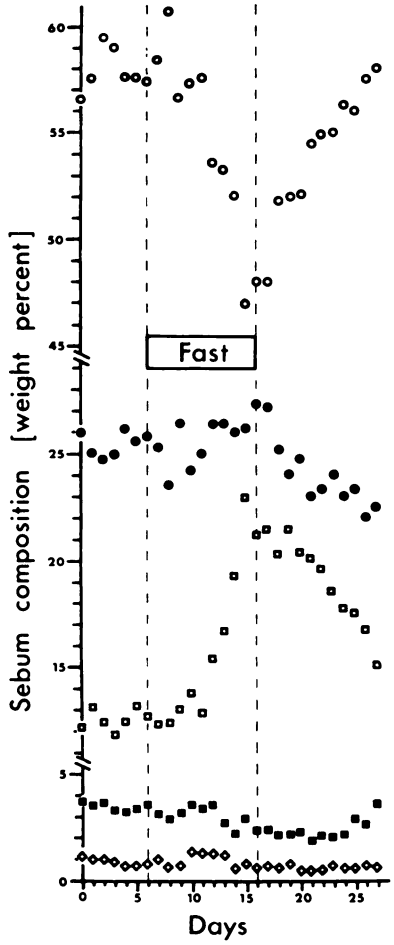

FIG. 1. Average forehead surface lipid composition for four normal human subjects during starvation. ○ = combined triglycerides, diglycerides, and free fatty acids; ● = wax esters; □ = squalene; ■ = cholesterol esters; ◇ = cholesterol.

are similar to the results obtained previously in obese subjects (4). In our previous study, gravimetric measurement of the rate of lipid excretion from the skin showed that sebum production was reduced by 40% during starvation, and that the reduction was produced by suppression of the synthesis of triglycerides (−39%), wax esters (−45%), and cholesterol and its esters (−55%), whereas squalene synthesis remained virtually unchanged (+3%). In the present instance, if squalene is assumed to remain constant in amount, it is possible to calculate the absolute change in other constituents required to produce the change in sebum composition resulting from fasting. For the average lipid composition at the point of maximum change, the magnitudes of suppression of wax esters (−44%) and cholesterol and its esters (−52%) are similar to those obtained with obese subjects, although the suppression of triglycerides (−55%) is somewhat greater.

The skin surface lipid is derived from two sources, the epidermis and the sebaceous glands. Squalene and wax esters are of sebaceous gland origin; cholesterol and cholesterol esters are primarily from the epidermis; and triglycerides are derived from both the epidermis and the sebaceous gland. Thus, the composition of the surface sebum will depend upon the sebaceous gland contribution in the region of skin studied (1). In the present experiments, the samples were taken from the forehead, an area where 95% of the lipid is sebaceous in origin; therefore it can be assumed that the observed changes are occurring in the sebaceous glands. Sebaceous lipids are formed in the glands and not absorbed from the blood; wax esters and squalene are not found in blood. Moreover, the double-bond position in the unsaturated fatty acids of blood have a Δ^9-unsaturation pattern, whereas Δ^6-unsaturation is predominant in the cutaneous lipids.

At present there is no explanation for the observed phenomenon, and it is not known whether other catabolic states would show a similar effect. It is unlikely, however, that the observed changes reflect enhanced utilization of substrate to furnish energy because squalene, as well as the other lipids, is formed from acetate.

It is apparent that the increase in the squalene concentration in sebum as the result of fasting is not limited to obese subjects. The suppression of sebaceous synthesis of all lipids except squalene therefore appears to be a specific effect of starvation. Gross disturbances of nutrition must be considered as a factor in experiments in which analyses of skin surface lipids are performed. It is possible to contemplate the use of surface lipid analysis in the study and diagnosis of nutritional disorders.

Summary

After 5 days without food, human subjects showed a marked change in sebaceous gland

composition of the forehead skin lipid, apparently as the result of suppression of the synthesis of all lipids except squalene in the sebaceous glands. The change was reversed by return to a normal diet.

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