

## FURTHER OBSERVATIONS ON THE USE OF LIPOCAIC IN THE TREATMENT OF PSORIASIS\*

EDMUND N. WALSH, M.D.

*Whiting, Indiana*

D. E. CLARK, M.S., M.D., L. R. DRAGSTEDT, Ph.D., M.D., AND  
S. WILLIAM BECKER, M.S., M.D.

*Chicago*

(Received for publication June 11, 1940)

In a previous report (1), preliminary observations on the treatment of six psoriatic patients by means of lipocaic were presented. Four of these patients showed marked improvement and two failed to respond. The improvement seemed to coincide with a lowering of the blood lipid level which had been found to be elevated in three of the patients. Further observations on these six patients and an additional seventeen patients form the basis of this report.

Lipocaic (2) is a hormone contained in a defatted alcoholic extract of the pancreas which appears to play some role in the metabolism or transport of fat. When given to depancreatized dogs which are receiving insulin and are on a normal diet, it prevents the fatty infiltration of the liver which usually develops in these animals. However, if the dogs are fed a fat free diet lipocaic is not required to prevent this change. Its use in psoriasis was suggested by the well known contention of some investigators that this disease is the result of a deranged fat

\* Read before the 3rd Annual Meeting of the Society for Investigative Dermatology, New York, June 11, 1940.

This work has been aided by grants from the Josiah Macy, Jr. Foundation, the Douglas Smith Foundation for Medical Research of the University of Chicago, The Eli Lilly Company, and the Committee on Research in Endocrinology of the National Research Council.

From the Department of Surgery, and the Section of Dermatology of the Department of Medicine, the University of Chicago.

metabolism, and the fact that lipocaic has been found to reduce the abnormally high blood lipids found in persons with xanthoma.

In the present study, twenty-three patients were observed for from two to eighteen months. There were eight women and fifteen men; their ages ranged from ten to sixty-seven years. The patients were selected chiefly on their willingness to cooperate. They presented lesions of all types which had been present for from seven months to many years. About half of them had a fairly generalized eruption and in one quarter it was of recent onset or represented exacerbation of chronic psoriasis. The remainder had lesions of varying severity on the usual sites of predilection, namely, the elbows, knees, scalp and sacral region.

Treatment consisted at first only of the administration of lipocaic capsules. Each contained one-half gram of pancreatic extract which was equivalent to twenty-five grams of raw pancreas. The dosage per day ranged from eight to twenty-eight capsules. Later, in some cases which responded slowly or not at all to lipocaic, five per cent crude coal tar ointment, or 0.10–0.25 per cent anthraline ointment were used on all lesions except those on the scalp where five or ten per cent ammoniated mercury was applied. The patients returned at two to four week intervals and blood was drawn for the determination of the total fasting blood serum lipids by gravimetric analysis.

The present data do not bear out some of the tentative conclusions in the first report. Lipocaic does not, as was first thought, tend to lower the blood lipid level in psoriatic patients nor is improvement of the psoriasis necessarily accompanied by any change in the level of the blood lipids. Thus, if lipocaic does influence psoriasis through a change in the blood lipids, it probably is a qualitative and not a quantitative change.

To determine whether or not a treatment of psoriasis which depends chiefly on crude coal tar causes any change in the blood lipid level, a patient, who had previously received lipocaic without effect, was hospitalized and treated with 5 per cent crude coal tar ointment, ultraviolet light, autohemic injections and mild sedation. The psoriasis cleared completely in four weeks but there was no significant change in the level of the blood lipids.

That crude coal tar, which is an effective drug in the treatment of psoriasis may also produce its effect through qualitative alteration in the blood fats when applied locally, is suggested by the following work of Hansen (3). It was found that the blood fats in children with infantile eczema had an abnormally low iodine number, i.e., contained less than the normal percentage of unsaturated fatty acids. When crude coal tar ointment was applied locally to the eruption, there was a rise in the percentage of unsaturated fatty acids in the blood as indicated by an increase in the iodine number. This change was concurrent with clinical improvement of the eczema.

## RESULTS OF TREATMENT

However, that there does seem to be some correlation between the blood lipid level and the response to lipocaic therapy is brought out in table 1.

TABLE 1

	TREATMENT WITH LIPOCAIC ALONE, 22 PATIENTS			TREATMENT WITH LIPOCAIC PLUS LOCAL APPLICATION, 12 PATIENTS		
	Cleared	Improved	No change	Cleared	Improved	No change
No. of cases.....	7	11	4	3	6	3
Per cent.....	31.8	50.0	18.2	25	50	25
Average blood lipid..	656	796	833	721	783	896

The table shows the results for the period when the patients were receiving lipocaic alone and also for the combined treatment period. The average blood lipid of the patients whose eruption cleared with lipocaic (656 mg. per cent) was much lower than that of any other group. Those who were not benefited by lipocaic even when combined with local applications showed the highest average level (896 mg. per cent). Patients who improved or were entirely refractory to lipocaic treatment and those that cleared or improved with combined treatment showed intermediate values (796, 833, 721 and 783 mg. per cent respectively). In all, 31 per cent were cleared, 51 per cent improved and 18 per cent showed no change with lipocaic alone.

If 750 mg. per cent is considered to be the upper limit of the normal range for fasting blood lipids by the method used, 13 or 56 per cent of the patients had an abnormally high level. These 13 patients include only one of the group which cleared with lipocaic alone (763 mg. per cent). Another rather striking correlation was noted between the blood lipid level and the age of the patients. They were divided arbitrarily into two groups, those thirty years of age and under and those over thirty. The younger group (11 patients) had an average blood lipid of 678 mg. per cent and included five of the seven patients whose eruptions cleared with lipocaic alone. The older group (12 patients) had an average of 833 mg. per cent and included all of the patients whose eruptions showed no response to either treatment.

Besides this apparent relationship between the blood lipid level and the effect of lipocaic in improving psoriasis, there are several other observations which indicate that this substance has a specific action on the disease. In practically all the cases, there was a change in the character of the scales during the first two to four weeks of treatment. They became finer and drier and in many cases decreased in amount. At the same time the lesions often became paler and less elevated. Secondly, the improvement usually was effected during the winter months when psoriasis tends to become worse. Thirdly, the three patients who were cleared by using both lipocaic and local applications found that neither alone would keep them free from lesions.

Special mention in some detail should be made of the further course of the six patients originally reported. They have now been under observation from 12 to 18 months, four of them through two winters. In the four patients whose skin cleared with lipocaic alone, the capsules were stopped in April or May 1939 and they were considered "cured" even though some still had very small lesions on the elbows or knees. All four have had recurrences. One occurred in July and the lesions disappeared in two weeks when six capsules a day were taken. The same patient had a more severe recurrence in January 1940 but with larger doses of lipocaic the lesions went through the same changes mentioned above and her skin cleared gradually. Another patient returned with a severe recurrence in September

1939. She was started on lipocaic and in eight weeks showed the usual change with central clearing. She was unable to continue treatment at that time and when last heard from she had had an extensive eruption all during the winter and spring. The two remaining patients who were benefited returned in November 1939 and March 1940 with a few lesions. These improved after administration of lipocaic, although the patients continued to have a few small pale lesions which would come and go from week to week. Thus lipocaic seems to be equally effective when used for treatment of recurrences in contrast to many anti-psoriatic remedies which are less effective in the treatment of recurrences than when used for the first time.

The two patients who were not helped by lipocaic alone both returned in the fall because the psoriasis had gotten worse. We again gave lipocaic but in larger doses. One whose average blood lipid level was 690 mg. per cent was entirely clear in February. The other with an average blood lipid of 1003 mg. per cent has not responded to any ambulatory treatment including ultraviolet light, crude coal tar ointment and x-ray.

Another patient deserving special consideration was a 10 year old girl who had been under observation for five years, most of that time having been spent in a hospital. She had a dermatitis, most severe on the face, scalp, arms and legs but at times generalized, which was characterized by erythema, scaling and crusting. It had been diagnosed by various dermatologists as seborrheic dermatitis, seborrheic psoriasis, pustular psoriasis and "psoriasoid." Treatment of all types had been tried but the disease had never been cured. The average blood lipid level was 821 mg. per cent. She was started on lipociac and immediate improvement was noted in the skin. The drug has been stopped several times and each time an exacerbation occurred. No change was produced in the blood lipid level.

Little is known about the effects of large doses of lipociac since its exact role in the metabolic processes is not known. In general there was no effect on the patients' health or weight. Several stated that they felt better when taking the drug. Over half of the patients noted a laxative effect especially with the higher doses. This was probably due to the relatively large amount

of inorganic salts, principally  $\text{NaSO}_4$ , which remains from the extracting process. Some patients experienced mild abdominal cramps after taking the capsules, probably for the same reason. There was no correlation between the laxative effect and the skin changes. One patient, while taking 25 capsules a day, developed dizziness, weakness, nausea, vomiting and diarrhea. Discontinuance of the drug relieved the symptoms entirely. One patient developed amyotrophic lateral sclerosis while taking lipocaic, which seems to have been an entirely coincidental occurrence.

#### COMMENT

The many points on which this study is open to criticism are fully realized. For a disease which is subject to as definite spontaneous and seasonal variations as psoriasis, this is a relatively small series of patients observed over a short period of time. The lipocaic used was by no means a pure product, could not be accurately standardized, and may have varied considerably in potency. No control series using sodium sulfate alone or some entirely inert substance was observed. Nevertheless, despite these shortcomings, it is felt, for the reasons stated above, that these data do support the contention that psoriasis is in some way related to lipid metabolism, possibly through both a quantitative and qualitative alteration in the blood lipids. Also, some factor in the material given these patients, probably lipocaic, has a definite beneficial effect on psoriatic lesions which is more evident in patients with a low fasting blood lipid level.

It is hoped that through further study of the lipid chemistry of these patients by determinations of lipid fractions, cholesterol tolerance curves, iodine number, the effect of fat free diets, the effect of Vitamin D on the blood lipids, etc., more light can be shed both on the mode of action of lipocaic and the underlying cause of psoriasis.

#### SUMMARY

In twenty-three psoriatic patients observed for from two to eighteen months who were treated by the oral administration of lipocaic alone, clearing of the lesions occurred in 31 per cent, improvement in 50 per cent and no change in 19 per cent.

Lipocaic did not cause a reduction of the blood lipid level in patients with psoriasis as had first been thought but patients with a low blood lipid cleared more readily with lipocaic or lipocaic plus local treatment than those with high blood lipid levels.

Younger patients had a lower average blood lipid than those in the older age group.

Lipocaic causes a drier and finer type of scaling from psoriatic lesions.

The data presented supports the belief that psoriasis is in some way a manifestation of a disturbed lipid metabolism.

#### BIBLIOGRAPHY

- (1) STEWART, C. D., CLARK, D. E., DRAGSTEDT, L. R., AND BECKER, S. W.: The experimental use of lipocaic in the treatment of psoriasis. *JOUR. OF INVESTIGATIVE DERMATOLOGY*, **2**: 219, 1939.
- (2a) DRAGSTEDT, L. R., VAN PROHASKA, J., AND HARMS, H. P.: Observations on a substance in pancreas (a fat metabolizing hormone) which permits survival and prevents liver change in depancreatized dogs. *Amer. Jour. of Phys.*, **117**: 181, 1936.
- (2b) DRAGSTEDT, L. R.: The present status of lipocaic. *J. A. M. A.*, **114**: 29, 1940.
- (3) HANSEN, ARILD E.: Possible mechanism of crude coal tar therapy in infantile eczema. *Proceedings of the Society for Experimental Biology*, **31**: 161, 1933.

#### DISCUSSION

DR. ERICH URBACH, PHILADELPHIA: It is very interesting that lipocaic has proven of much value in the treatment of psoriasis.

At the International Dermatological Congress in Budapest (1935) I disagreed, as I still do, that psoriasis is basically a disturbance of lipid metabolism. Although it is true that a diet low in fats is one of the greatest helps at present in certain cases, the improvement can be mostly attributed to the resultant loss of weight as demonstrated by equally good results with other weight-reducing diets. Schamberg of Philadelphia showed this with a low protein diet, and during the World War we had the opportunity of seeing the startling effect of severe restrictions of diet on the incidence of psoriasis in Austria. Some years later, when food was plentiful, there was a marked increase in psoriasis.

There is no question but that there is some connection between diabetes and psoriasis and that carbohydrates and lipoids have something to do with psoriasis. I am inclined to believe that this connection is rather a complex one. It seems to me that psoriasis and metabolic disturbances do not stand in relationship of cause and effect but rather are components of a common mechanism, at present unknown.

DR. JOHN F. MADDEN, *St. Paul*: This has been a most interesting and unusual report. Although improvements and cures are very high—almost eighty per cent—a number of other things used for psoriasis have done equally well. The most interesting fact to me was that lipocaic not only controlled the disease when it was first used, but that it also controlled recurrence.

In a large series of cases over a number of years I have found many remedies, which would almost entirely control psoriasis the first time the remedy was used. When the patient had a recurrence the previously effective remedy often had no effect whatsoever.

Another point which, I think, Dr. Becker should bring out, is the fact that lipocaic is not generally available, and the reasons why it is not available.

DR. PAUL GROSS, *New York City*: As I pointed out in my paper, Gavin and McHenry have demonstrated in rats, that the lipotropic function of lipocaic is also present in rice polish concentrate and Brewer's yeast. This will explain the good results which I obtained recently in two cases of psoriatic erythroderma by injections of liver extract. One was a case of generalized psoriatic erythroderma in an old lady, of two years duration. The erythroderma cleared up but the patches of psoriasis remained. After continuous therapy with oral administration of liver extract, even the more resistant lesions disappeared, recently. The other case, was one seen at the Presbyterian Hospital only a short while ago. It was a case of gold dermatitis in a patient suffering from psoriasis and arthropathy. The generalized gold dermatitis was transformed into a psoriatic erythroderma, but under intensive liver therapy, not only the erythroderma cleared up completely, but even old psoriatic lesions disappeared temporarily. It is interesting to note that liver therapy for psoriasis was recommended more than ten years ago.

DR. LAWRENCE C. GOLDBERG, *Cincinnati*: Would we obtain the same results as are obtained with Lipocaic if we gave the patient fresh whole pancreas? This might be advisable inasmuch as the material is unavailable at this time.

DR. HAMILTON MONTGOMERY, *Rochester, Minnesota*: I have seen several cases where one or two members in a family had psoriasis and yet had normal or low blood plasma lipoids and a third member had marked increase in all the blood plasma lipoids. The majority of cases of psoriasis show no appreciable change either relative or quantitative in the various blood plasma lipoids. Practically all patients with psoriasis, almost without exception, respond satisfactorily to treatment as outlined by Dr. Goeckerman using crude coal tar and ultraviolet light. This method of treatment works equally well the second and third time as it does the first time. The response to crude coal tar and ultraviolet light treatment does not vary according to the blood plasma lipoids of the individual case. Dr. Brunsting has had distinct success in quite a few cases of psoriasis treated with large doses of vitamin D. We have not had any experience in the use of lipocaic inasmuch as it has been difficult to obtain in sufficient amounts.

DR. M. H. GOODMAN, *Baltimore*: From the work of Urbach and Madsen, disturbance of fat metabolism in psoriasis cannot be spelled in terms of quantitative measurements of lipoids in the blood. It would be interesting to know what

proportion of the individuals treated with lipocaic were obese, and what proportion were thin.

In the work of both Urbach and Madsen, it is not so much quantitative difference in lipid content of the blood, but rather the shift in the metabolism of fat which seems to affect or influence favorably the individual with psoriasis. It would seem that if lipocaic, in some manner, produces an alteration in fat metabolism the obese psoriatic would profit from it in the same way as he might from a low fat diet.

DR. THEODORE CORNBLEET, *Chicago*: From my investigations, it appears that the glycogen content of the skin in psoriasis is raised above and the glucose level depressed below that found in the normal skin. Without further information it cannot be said that these findings are related to the cause of psoriasis, result from it, or merely incidental. The same may be said about the altered blood lipid pattern commonly found in psoriasis. Carbohydrate and fat metabolism can be related and alterations in both are well known in disease, as in diabetes. Similarly, some interrelationship may be present in psoriasis. My feeling about the purely fat metabolic theory of psoriasis, however, is that the changes are not sufficiently consistent to be of etiologic significance. For this reason, while I hope lipocaic is what all of us are seeking for the use against the scourge of psoriasis, my belief is that as an attack on the deranged fat metabolism, it will prove to be only a partial aid in some cases.

DR. S. WILLIAM BECKER, *Chicago*: I appreciate this discussion. You realize the difficulties under which we are laboring.

We know that lipocaic does regulate lipids because depancreatized dogs treated with insulin will always die with fatty livers if they are kept on a normal diet unless they are given whole pancreas or a similar material. Treatment by lipocaic is not presented as the best therapy. Dr. Goeckerman's combination has, in our experience, given about one hundred per cent results, but it practically means hospitalization. In answer to Doctor Madden, lipocaic is not available because it is made for experimental use, and when the manufacturers make lipocaic it is necessary to stop the production of insulin and use the apparatus for making lipocaic. They are now doing experimental work on the residue to see whether lipocaic can be obtained from it.

It is difficult to be sure that lipocaic is present in a pancreatic extract. The only sure way to assay lipocaic in a given material is to give it to depancreatized dogs. The dogs should also be given insulin, and if they do not die, then we may be certain that lipocaic is present in the material. This is a long drawn out and unsatisfactory procedure, but it is the best we have at present. We have had no experience in the feeding of fresh whole pancreas.

In reply to Dr. Goodman, most patients have been rather thin. We have had no opportunity to observe the clearing of psoriatic eruptions following the use of Fowler's solution. I have never seen as spectacular changes in a psoriatic eruption without therapy. Lesions heal in the center and eventually the entire eruption disappears in some patients.

We feel that if lipocaic is only an adjunct to other treatments for psoriasis, it is a very convenient therapeutic measure, is taken simply by mouth, and we hope that when it is made available in the not too distant future it may be of help in the management of this extremely stubborn disease.