Trends in the Treatment of Acne Vulgaris

NATHAN PENSKY, M.D., and
NATALIE GOLDBERG, M.D.
Brooklyn, New York

ACNE VULGARIS is probably the most frequent cutaneous disease seen by physicians. Yet opinion differs greatly concerning the etiology and specific treatment for this cosmetically annoying and psychologically crippling disease. The clinician is often confused by the voluminous discussions and conflicting reports in the medical literature.

ETIOLOGY

According to Sulzberger and Baer,[1] clinical and experimental research indicates that the primary mechanism in the development of acne vulgaris is probably endocrine in nature – principally an imbalance between androgenic and estrogenic substances with the emphasis on an androgenic preponderance. White and associates,[2] however, feel that "The literature fails to reveal a definitive experimental basis for this theory. A review of the work of several investigators demonstrates the need for further work and more knowledge along these lines." They performed urinary 17-ketosteroid assays on 26 young men with acne vulgaris and found no evidence to substantiate the concept that the condition is related to an excess of androgenic hormone.

Sutton, Jr.[3] feels that acne vulgaris is a systemic disorder of endocrine and metabolic function "wherein the sebaceous glands are the seat of the clinically conspicuous dysfunction." Brunsting[4] states, "We speak of this (endocrine mechanism) rather glibly, yet do not understand the exact mechanism and all the implications. There may be wide variation in the ranges even in the apparently normal person without acne. Therapeutically our attempts in restoring this equilibrium have been equivocal." It is recognized that many other mechanisms, many of which are yet unknown, convert this endocrine dysfunction into a full-blown entity.

NATHAN PENSKY, *a 1933 graduate of George Washington University School of Medicine, is a specialist in dermatology in Brooklyn, New York.* NATALIE GOLDBERG, *a 1930 graduate of New York Medical College, Flower and Fifth Avenue Hospitals, also specializes in dermatology in Brooklyn.*

ANTIBIOTIC THERAPY

The role of pyogenic organisms in the acne complex leads to much speculation and disagreement. Peck[4] feels that bacteria play an important part in its development by acting either as sensitizing antigens or as direct infecting agents. He bases his contention on the many instances in which acne lesions have involuted after the parenteral administration of antibiotics and/or the oral and local use of broad spectrum bactericidal agents. Sutton, Jr.,[4] however, feels that bacteria, when present, are purely coincidental.

In treating severe cystic and pustular acne we use oxytetracycline (Terramycin). Our choice of antibiotic is based on the work of Welch,[5] Goldberg,[6] and Ritchie and Wallace.[7] Welch[5] studied the distribution of oxytetracycline in the tissues of the rabbit and found a much higher concentration of the antibiotic in the skin than in the blood. Goldberg[6] presented evidence that the oral administration of oxytetracycline caused involution of cystic and pyodermic lesions in acne vulgaris. Ritchie and Wallace[7] treated 50 children with burns and scalds with oxytetracycline and found no evidence of established infection using this type of prophylactic therapy.

Our immediate results in treating severe cystic and pustular acne routinely with oxytetracycline were encouraging, and so we enlarged our series to include 55 patients. They varied in age from 12 to 45 years; 30 of the patients were female. We tried to establish the smallest dose of the drug which would cause involution of the cystic and pustular elements.[8] We soon discovered that to control some individuals required 1 to 2 gm. a day, while others responded to as little as 0.5 gm. Some of our patients were maintained on oxytetracycline for as long as fourteen months.

However, our long-range results were disappointing. The pustular and infected cystic ele-

Reprinted from THE JOURNAL-LANCET, Minneapolis, November 1955, Vol. 75, No. 11

ments promptly reappeared and often became worse as soon as the medication was discontinued. In addition, unpleasant side reactions developed in 13 of our patients. The symptoms consisted of vaginal and rectal pruritus, diarrhea, nausea, and abdominal cramps. Therefore, we question the use of this broad-spectrum antibiotic over long periods of time. Although the severity of the reactions depended largely on the total daily dose, we noted reactions in patients who received as little as 200 mg. a day.

As a result of our experiences, we have discontinued the routine use of broad-spectrum oral antibiotics and reserve their employment solely for the severe pyodermic phase. We administer them only in the hope that we may obtain a remission of the symptoms while we utilize other modes of treatment.

LIVER THERAPY

According to Peck and associates,[4] the average case of acne runs a course of three to five years. However, in reviewing the histories of our acne patients, especially the older ones, we have found that many have had acne for a much longer period and that the condition is still severe.

In an attempt to shorten the duration of this condition and thus lessen its sequelae, we investigated other methods of treatment. We became intrigued by the use of liver preparations in the control of acne. Over the years, a considerable number of observers have tried this material. The results varied but in general they were encouraging. Sutton[9] felt that crude liver extract was beneficial. Hume[10] felt it was effective as an adjunctive measure in the therapy of acne. Walters[11] found that crude liver extract heated or unheated was beneficial. Lewis[12] stated that crude liver extract is sometimes beneficial even when no anemia is present. Marshall and Schadeberg[13] and Lichtenstein and Stillians[14] obtained good results with a fractionated derivative from crude liver.

Nierman[15] obtained definite improvement using Kutapressin in the treatment of 22 patients with cystic acne. Kutapressin is prepared from crude liver extract by a series of fractionations which concentrate the active principle ("S" factor) and render it better tolerated than even the purified extracts. In the process of fractionation, both the hypertensive and hypotensive principles of liver are removed. Kutapressin causes vasoconstriction of peripheral vessels and enhances the action of epinephrine on the smooth muscle cells in the terminal blood vessels, particularly those in the skin.[16]

In 1953, we reported our results using Kutapressin in the treatment of refractory acne.[17] Kutapressin was used to treat 52 private patients who had failed to respond to all other forms of treatment. We obtained moderate to good improvement in 63 per cent of our patients. Burks, Jr., and Knox[18] treated 226 patients with this "S" factor of liver supplied as Kutapressin. They employed a minimum of supportive treatment and reported 54.7 per cent moderate to pronounced inhibition of the disease.

Since our previous report,[17] we have extended the use of Kutapressin in the treatment of all forms of acne vulgaris to 72 additional patients, 41 of whom are female. They have been followed for a minimum of ten weeks; many have been observed for over eighteen months. In spite of the fact that 22 had received all forms of treatment including x-ray therapy elsewhere, their acne continued to blossom. All received biweekly injections of Kutapressin subcutaneously. The dose was 2 to 3 cc. In addition, all patients were treated with local modalities such as cryotherapy. Our impression, which was confirmed by the comments of the patients, was that clinical improvement became apparent in about six weeks and thereafter continued slowly but noticeably.

Statistically, improvement was impossible to evaluate as each case was a distinct entity and no 2 cases looked the same clinically. However, there was no doubt that the improvement was in some measure due to the liver therapy and not to spontaneous clearing. We agree with Burks, Jr., and Knox[18] that studies should be made to isolate the "S" fraction. Used in pure form in massive doses, more spectacular results might be obtainable.

Perhaps one of the actions of the "S" factor in liver is dependent upon its peripheral vasoconstricting effect. It may tend to prevent the outpouring of sweat which, according to Sulzberger,[1] could cause maceration and swelling of the keratin layer of the skin and thus cause plugging of the follicular openings.

FOOD FACTORS

The apparently normal individual can usually ingest most types of food without an acneform eruption. However, with some degree of regularity the symptoms of those with acne are aggravated by the ingestion of chocolate, cheese, shellfish, and nuts. Testing to prove susceptibility is of no value. The exact mechanism of this aggravation is not understood. As a matter of routine we eliminate chocolate, nuts, and sea food from the diet of these patients.

1955

DRUG FACTORS

Iodides and bromides often cause existing acne to flare. They may also cause an acneform eruption in normal individuals. Opinions differ in this regard. Some capable investigators have even reported beneficial results due to the intake of iodine. Perhaps the differences can be reconciled if we consider the section in which the patient resides. Iodine may be helpful in the Great Lakes region where intake of iodine is inadequate and where hypothyroidism exists. In normal iodine intake areas, an excess may cause a flare-up. Sutton and Sutton[19] state that sensitivity of acne patients to iodides is due to hypothyroidism and that when iodides and thyroid extract are given to a hypothyroid patient, an eruption does not occur.

EMOTIONAL FACTORS

While little is known about the effect of the autonomic system on sebaceous glands, it is recognized that emotional factors may precipitate exacerbations of acne vulgaris. The physiologic functions of the skin are under the influence of the autonomic nervous system, and quite possibly emotional factors influence acne vulgaris through this medium. Sulzberger[1] states that "Among the known mechanisms by which emotional factors could conceivably affect acne vulgaris are the demonstrated influences of nervous mechanisms on growth of secreting sebaceous elements, the easily demonstrable production of congestion through vasodilatation in the 'flush area' of the face and the undeniably strong and rapid effects on sweating. The swelling of the horny layer which repeated outpouring of sweat produces could possibly lead to constriction and plugging of the follicle openings and thus also lead to the formation of new acne lesions in a manner somewhat similar to that which is postulated in the production of lesions in 'tropical acne.'"

Emotional factors may be sufficient to "push over" potential acne lesions into actual lesions. While the emotional state of the patient may affect acne, the embarrassment of facial disfigurement and its consequent disappointments may have a profound effect upon the psyche and the emotional state of the emotionally unstable adolescent.

Sweating is an important factor in acne and free sweating should be discouraged, for increased sweating also increases sebum secretion. It is common knowledge that young men who exercise vigorously are more disposed to acne eruptions than those individuals who live a sedentary life.

VITAMINS

Vitamin A regulates the cornification of the skin. Good results have been described utilizing large doses of this substance. We have found this remedy very disappointing.

X-RAY THERAPY

In the discussion of Peck's paper on the treatment of acne with estrone, Eichenlaub[4] stated, "Personally I think that properly used, x-ray is going to be much less harmful to the patient in the end than the prolonged use of antibiotics or the prolonged use of estrogens." Peck[4] responded that he was perfectly happy with its use and he felt it was quite safe in the hands of those who know how to use x-ray.

We feel that x-ray therapy, if used by experts, is perhaps the best modality. It shortens the acne duration better than any other single therapeutic procedure. We limit the use of x-ray to patients over 18 years of age who have not responded well to a combination of other treatments. We have never experienced trouble with its use.

LOCAL TREATMENT

Routinely the patient is instructed to use plenty of soap and water. A flesh colored shake lotion with 2 to 5 per cent Resorcin and sulfur or a 3 per cent Resorcin-salicylic acid-alcoholic solution is used. This controls the associated seborrhea and the mild desquamation is also beneficial.

The use of powdered carbon dioxide in acetone to form a slush (cryotherapy) is especially indicated in cystic acne. When used carefully, it helps resolution of some of the cystic components and at the same time causes some peeling of the skin which is helpful.

ENDOCRINE

The use of hormones in the treatment of acne vulgaris is both praised and damned. Locally either sodium estrone sulfonate or diethylstilbestrol has been used as a cream by Peck and associates,[4] Shapiro,[20] Sawicky and associates,[21] and Philip.[22]

Becker[4] saw no difference between a placebo lotion and a lotion containing hormone. Sulzberger and Witten[23] believe that the use of hormones parenterally, orally, or topically has proved of only partial value in the management of acne. Eichenlaub[4] found their use locally and internally very disappointing.

We have not been very successful with either diethylstilbestrol or Premarin. However, an occasional case of premenstrual or chin acne ac-

companied by irregular periods has shown temporary improvement when Premarin in doses of 0.625 mg. has been given after ovulation and continued until menstruation has occurred.

THYROID EXTRACT

Sutton and Sutton[19] state, "Thyroid extract is indicated in all cases; it is given to tolerance without regard to B.M.R. or blood chemistry." They feel that thyroid extract is especially needed if the patient is depressed, fatigues readily, is anemic, and feels cold. They usually give 2 gr. of desiccated whole gland substance with the evening meal. Occasionally patients are given additional doses after breakfast and lunch. They prefer desiccated whole gland to thyroid extract. They state further, "The dose must be estimated by clinical trial, giving just less than the amount which produces symptoms of excess. The dose must be adequate." The dose may be decreased to one-half after two weeks.

Terramycin tablets and capsules were supplied in part by Chas. Pfizer & Co., Inc. and purchased in part by patients on prescription.
Kutapressin was supplied by Kremers-Urban Co.

REFERENCES

1. Sulzberger, Marion B., and Baer, R. L.: Yearbook of Dermatology and Syphilology. Chicago: Yearbook Publishers, Inc., 1949, pages 9-39.
2. White, Claude B., Peterson, Addelia, and Neff, Jane, C.: Acne vulgaris and urinary 17-ketosteroids in young men. U. S. Armed Forces M. J. 3:131-137, 1952.
3. Sutton, Richard L., Jr.: Treatment of acne vulgaris; experimental use of cortisone in acne and rosacea. J. Missouri M. A. 49:471-474, 1952.
4. Peck, Samuel M., Klarmann, Emil G., and Spoor, Herbert J.: Treatment of acne vulgaris with estrone. Arch. Dermat. & Syph. 70:452-467, 1954. — Discussion following presentation of paper by Peck, et al. (abstract). Sutton, Richard L., Jr., Eichenlaub, Frank L., Brunsting, Henry A., Beinhauer, Lawrence G., Becker, Frederic T., and Peck, Samuel M.
5. Welch, Henry: Absorption, excretion and distribution of Terramycin. Ann. New York Acad. Sc. 53:253-265, 1950.
6. Goldberg, Natalie D.: Management of acne cysts. J. Am. M. Women's A. 6:349, 1951.
7. Ritchie, H. D., and Wallace, A. B.: Terramycin therapy in burns. Antibiotics & Chemother. 2:394-398, 1952.
8. Pensky, Nathan, and Goldberg, Natalie D.: Unpublished data.
9. Sutton, Richard L.: Liver diet in acne vulgaris and in furunculosis. Arch. Dermat. & Syph. 18:887, 1928.
10. Hume, E. B.: Treatment of acne rosacea. Am. Pract. 2:324-326, 1948.
11. Walters, J. D.: Collateral findings and supportive therapy in acne vulgaris. Ohio State M. J. 44:697-699, 1948.
12. Lewis, George M.: Practical Dermatology for Medical Students and General Practitioners. Philadelphia: W. B. Saunders Co., 1952, 13 pages.
13. Marshall, Wallace, and Schadeberg, William: Study of keloids and related conditions. Wisconsin M. J. 49:369-373, 1950.
14. Lichtenstein, M. R., and Stillians, Arthur W.: Liver extract in treatment of acne vulgaris in tuberculous patients. Arch. Dermat. & Syph. 45:959-962, 1942.
15. Nierman, M. Murray: Treatment of cystic acne vulgaris with cutaneous vasoconstrictor (Kutapressin). J. Indiana M. A. 45:497-502, 1952.
16. Lee, Richard: To be published.
17. Pensky, Nathan, and Goldberg, Natalie: Treatment of refractory acne with a fractionated type of liver extract. New York State J. Med. 53:2238, 1953.
18. Burks, James W., Jr., and Knox, John M.: S-factor of liver extract in acne vulgaris. Arch. Dermat. & Syph. 70:508-510, 1954.
19. Sutton, Richard L., and Sutton, Richard L., Jr.: An Introduction to Dermatology. St. Louis: C. V. Mosby Co., 1941, pages 246-263.
20. Shapiro, Irving: Estrogens by local application in treatment of acne vulgaris. Arch. Dermat. & Syph. 63:224-227, 1951.
21. Sawicky, H. H., Danto, Julius L., and Madden, W. Stuart: Clinical evaluation of topically applied estrogen cream in acne vulgaris. Arch. Dermat. & Syph. 68:17, 1953.
22. Philip, Arthur J.: Topical estrogens in acne vulgaris. New York J. Med. 51:1313-1314, 1951.
23. Sulzberger, Marion B., and Witten, Victor H.: Hormones and acne vulgaris. M. Clin. North America 35:373-390, 1951.