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Current therapy for acne vulgaris

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THE CURRENT THERAPY FOR ACNE VULGARIS

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Chapter I

INTRODUCTION

"It is for homely features to keep home,--
They had their name thence; coarse complexions
And cheeks of sorry grain will serve to ply
The sampler, and to tease the huswife's wool.
What need a vermeil-tinctur'd lip for that,
Love darting eyes, or tresses like the morn?"
--Milton's "Comus"

Acne vulgaris is one of the classic dermatologic signs of puberty, and it may be observed in slight to marked degree in 80 per cent of adolescents. It may manifest itself as only a passing disturbance which produces no sequelae, or it may become severe and extensive, with secondary infection, scarring and marked derangement of the adnexal structures of the skin.

There has been increasing interest in acne on the part of commercial pharmaceutical concerns, and this has, in turn, led to a more active search for improved therapeutic and cosmetically acceptable dermatologic preparations. This is evident from the ever-increasing numbers and varieties of proprietary therapeutic agents prepared by cosmetic concerns and now available "over the counter"

to teenagers and others afflicted with acne. It is further borne out by the stepped-up advertising through the media of television, radio, magazines, periodicals and the lay press. It may be convenient and gratifying for acne sufferers to purchase helpful, relatively harmless and cosmetically acceptable proprietary preparations without the prescription of a physician. However, the inevitable enthusiasm of some advertising agencies has highly exaggerated the real benefits which can be derived from these over-the-counter preparations and has even resulted in some half truths, distortions and at times untruths.

Nevertheless, as is sometimes the case, with the bad there may come some good; and so, indeed, the publicity for proprietary preparations on television, on radio and in the press may be of some help in instilling a more hopeful attitude in those troubled with acne regarding possible benefits which can be expected from treatment. It is rare nowadays for a patient to seek professional help who has not already attempted some

do-it-yourself treatment with one or more of the available proprietary medications.

Along with these changes in attitude on the part of the general public, there has been a more understanding and helpful attitude on the part of the family physician. He can no longer shrug off the problem of acne with passing remarks such as "She'll outgrow it", "Have him scrub often with soap and water" and "Don't be so self-conscious - most of your friends have the same trouble". He must take a positive stand in treating the disease.

Why, then, all this concern over a disease which does not affect general health and, under ordinary circumstances, is not physically incapacitating or debilitating? Obviously, any eruption which affects the exposed parts of the body, particularly the face, and can be readily seen by all, is likely to be of deep concern not only to those who are affected but also to their immediate families and associates.

Active measures to combat acne are essential for the following reasons: (1) to keep the patient

socially presentable, and thus reduce or eliminate those psychological handicaps which so often burden patients with acne; (2) to prevent the development of the more serious extensive pustular and cystic forms of the disease; and (3) to prevent permanent scarring of the skin and of the psyche.

The proper management of acne depends on an understanding of the pathogenetic mechanisms involving the anatomic structure largely responsible for the disease, the pilosebaceous unit consisting of the sebaceous gland and its associated hair follicle. The sebaceous follicles are characterized by (1) widely dilated follicular canals filled with keratin, lipids and organisms, (2) massive multi-lobular sebaceous acini lying in the dermis, and (3) small inconspicuous lanugo hairs which cannot keep the follicle cleared out. The primary lesion of acne is the comedo (blackhead). Comedones removed from acne patients have been extracted with chloroform and separated into the chloroform-soluble extract and the residual keratinous material.

Suspensions of the latter injected intradermally into the acne patient reproduced lesions resembling those of pustular acne. Two types of comedones develop in the sebaceous follicles: (1) The clinical "blackhead" is an open comedo composed of an epithelium lined sac filled with horny lamellated material. The mouth is widely dilated, the contents can escape to the surface, and it rarely becomes inflamed. (2) "Whiteheads" are closed comedones and have a microscopic opening which keeps the contents from escaping, often becoming enflamed. The rupture of the walls of closed comedones leads to liberation of lipoids and horny material into surrounding dermis exciting a foreign-body reaction. These deep inflammatory lesions are often infected with *Corynebacterium acne*. Most of the superficial pustules occur in sebaceous follicles without comedones and start as small follicular breaks through which sebum escapes with resulting inflammation. Pustules also originate from the rupture of closed comedones or there may be a true bacterial impetigo of the follicle.

There are three major factors in inflammation.

(1) Injection of sebum leads to severe inflammation (the major inflammatory agent appears to be short-chained fatty acids); (2) Injection of keratin incites inflammation which is predominately of foreign body type with many giant cells; and (3) Injection of *Corynebacterium acnes* into keratinous cysts results in their rupture with massive inflammation.

Ideally the treatment of any disorder is to correct and eliminate the various etiologic factors. Unfortunately, this is not possible in the case of acne as the etiology of the condition has not yet been definitely established. The many heterogeneous factors playing a purported role in the pathogenesis of acne include heredity, puberty, endocrine disturbances, disturbances in water balance, hyperactivity of the parasympathetic nervous system, the psychogenic component, the allergic element, and exogenous substances such as iodine, bromine, coal tar derivatives, and oils. Many of the various therapeutic measures suggested are based on the

correction of one or more of these supposedly
etiological factors.

Chapter II
THERAPY OF ACNE VULGARIS

A. VACCINE AND TOXOID THERAPY

Perhaps one of the first scientific approaches to the treatment of acne vulgaris dates to the discovery by Paul Unna in 1893 of an organism which he isolated from acne lesions. This organism was called the acne bacillus or *Bacillus acnes*. Believing the acne bacillus, together with staphylococci, to be of etiological importance Fleming,⁵² in 1909 proposed that vaccines should be of value. He divided his acne cases into three classes for therapeutic purposes; first, those in which he believed the acne bacillus alone to be responsible; second, those in which both the acne bacillus and staphylococci were believed to be causative; and third, those in which staphylococci alone were believed responsible. He classified the cases by the appearance of the lesion and by microscopic

examination of smears from the lesions. The first group was given acne bacillus vaccine, the second mixed vaccine, and third staphylococcus vaccine. Doses varied from five to fifty million bacilli, usually about ten million, and up to 250 million staphylococci. Though there were some failures, he considers his results satisfactory. Usually, the pustules were temporarily aggravated, followed by marked improvement. Stock bacillary vaccine was satisfactory in some cases while autogenous vaccine was necessary in others.

Both Engman⁴⁷ and Gilchrist⁵⁹ in 1910 enthusiastically reported satisfactory results with vaccine therapy. Engman believed Fleming's dose too large and never used over three million bacilli at the initial vaccination. He repeated vaccination in five to seven days. In his opinion, this usually resulted in a cure; if not, a larger dose of seven to nine million was given. Gilchrist used x-ray with the vaccine but considered the former to be of little value except for decreasing skin oiliness. He considered vaccine therapy to be especially valuable in chronic, nodular, relapsing types.

Lovejoy⁹⁸ also achieved good results with vaccine therapy and believed stock vaccine to be as good as the autogenous. He also emphasized that the general health of the patient is of great importance, and treatment along this line might have been partly responsible for his favorable report.

However, not all reports were favorable. Morris and Dore¹²² disagreed with Engman as to the value of vaccine and expressed the belief that it is no more than a useful adjuvant of the ordinary form of treatment. They believed no true immunity was produced. Sequeira¹⁵⁶ and MacLeod and Topley¹⁰⁸ also found vaccine treatment disappointing, especially in the comedo type lesions believed to be caused chiefly by the acne bacillus. They reported occasional success in the pustular type believed to be due to staphylococci.

Dolman⁴¹ opened a new approach to the subject when he tried staphylococcal toxoid on several types of lesions in which staphylococci were believed to be involved. He used a preparation

detoxified with formalin. He reports what he thought was the cure of six patients with a severe pustular acne. However, a study using only six patients has insufficient value for use as an evaluation. It has been suggested by Downie⁴³ that the value of vaccines is due chiefly to the small amount of toxoid formed in their preparation. However, only one year later, in 1934, Dolman⁴² makes a somewhat pessimistic report on the use of toxoid therapy especially in acneform eruptions. He attributes this failure to the use of toxoid prepared from toxin of low antigenic potency. Kindel and Costello⁸⁹ achieved poor results with toxoid. In a series of 42 patients, 28 cases of acne, eight cases of sycosis vulgaris, and six cases of furunculosis, only eight cases were slightly improved and 34 were unimproved or worse at the end of the treatment. The belief was expressed by Jordan⁸³ in 1943 that neither vaccine nor toxoid alone was sufficient but rather, the dual stimulation of both antibacterial and antitoxic substances was necessary. Accordingly, she treated a group of

65 acne patients with a staphylococcal vaccine-toxoid. Of these, eight per cent showed no improvement, 14 per cent were slightly improved, and 60 per cent were decidedly improved or cured. She believed intracutaneous injections in small doses best to obtain maximum antigenic response with minimum dosages. However, she gave radiation treatment concurrently with the vaccine-toxoid in some cases. She states they had had x-ray treatment before with no benefit and therefore considers it not of major importance in the improvement. It is quite possible, though, that the previous radiation had been insufficient and this further radiation was all that was necessary for the improvement shown.

Macdonald and Taylor¹⁰³ concluded that staphylococcus toxoid was worthwhile only as supportive therapy during clinical trials in 1951. They gave toxoid to 34 females for periods up to 3 months and 23 showed improvement while a control group of 32 females showed 15 improved. However, both groups were given diet and skin cleansing rules.

James⁷⁸ in 1961, reports that he uses staphylococcus toxoid-vaccine routinely to control chronic infection and increase resistance to staphylococci by stimulating production of specific antibacterial antibodies as well as specific antitoxin formation.

B. ENDOCRINE THERAPY

Endocrine disturbances have been suspected as the cause of acne ever since the physiological importance of these glands has been recognized. Much evidence seems immediately apparent to support this idea. Acne has its onset predominantly during the adolescent period when the body is attempting to readjust its endocrine system for adult life. Its severity characteristically fluctuates with the female sexual cycle, exacerbations occurring premenstrually. Furthermore, acne almost always spontaneously clears or improves after the adolescent period is passed. Block¹⁷ has shown statistically that there exists between the start and cause of acne and puberty, not only a pronounced chronological, but also an

inner, causal connection with the endocrine system and, more specifically, the gonads. Because of its prevalence he regards acne as almost a physiological manifestation of the organism, at the time of puberty, which goes through a transition stage to become pathological.

In the earlier days of endocrine therapy many clinicians treated acne by means of the oral administration of the products then available, such as thyroid, ovarian, testicular and adrenal extracts. Their results were so uniformly discouraging that they are no longer popular. Following these discouraging results endocrine therapy fell into disuse. It was only natural, however, that when physiologically potent preparations became available interest would be resumed.

Although practically all of the hormones have been suspected as being of etiologic importance, only the sex hormones, male, female and gonadotrophic, appear to warrant much consideration.

Rosenthal et al.¹⁴³ investigated the comparative amounts of estrogenic substance in the urine of 34 female patients with acne. They found it was absent in twenty-seven, normal in six and decreased in one. They then treated a series of 38 acne patients by injections of estrogenic substance.¹⁴⁴ Of these, 13 definitely improved, 10 showed slight improvement and 15 failed to improve.

Van Studdiford¹⁸⁵ achieved somewhat better results in 15 patients treated with injections of estrogenic substance, 11 of whom improved. Hollander and Schmitt,⁷³ using an estrogenic hormone of placental origin on 41 females and ten males, noted a definitely good response in ten of the females and four of the males. Improvement, if it occurred, was always manifest by the end of the second month. Seven of the ten females had a definite association between the acne and the menstrual period. Only one of the 14 improved patients did not have an oily skin. Without exception, they report, the oiliness of the skin became much less while taking

the estrogenic hormone. After withdrawal of medication, relapses occurred in 11 of the 14 improved patients. This would appear to be of some significance though the percentage improved is not impressive.

Ingram⁷⁷ advocates the implantation of a crystal of oestradiol, 200 to 250 mg., suggesting that saturation of the system with estrogen is necessary to produce convincing results. He believes this particularly effective in severe pustular acne in the precocious young male and in those females where the acne appears to be associated with ovarian deficiency.

Lynch¹⁰¹ attempted local application of estradiol incorporated in a suitable base hoping for local improvement without systemic effects. Improvement was noted in 72 per cent of 79 female patients, but improvement was also noted in 63 per cent of 35 controls. This difference was not considered significant, especially since the result could be classified as definitely good in only 37 per cent of each group.

All this work, of course, has been based on the theory that acne is the result of estrogen deficiency, which is not necessarily so. Despite the results, which can be termed mediocre at best, this may yet prove to be a very important factor.

Much work has been done suggesting an excess of the physiologic antagonist of estrogen, the androgenic substances. It is presumed that if this is true, the adrenal is necessarily the source of the androgens, especially in the female. Wile et al.¹⁹⁵ found a moderate increase in the urinary excretion of androgen in patients of both sexes with acne. A decrease in the excretion of estrogen was also noted in both sexes. However, they did not feel their findings warranted indiscriminate or empiric therapeutic use of estrogens. They found no rationale for the use of androgens.

Hamilton⁶⁵ has observed that eunuchoid individuals, who do not mature sexually, never have acne. Upon administration of male hormone substance, testosterone propionate, to eunuchoid

and castrate men, prepubertal boys and ovariectomized women, comedones, papules and pustules developed in some. With termination of the hormone therapy, the acneiform responses diminished and began to disappear. Repetition of hormone administration and subsequent withdrawal again yielded the same results. He further noted, however, that if the testosterone propionate was continued in those individuals who developed acne with its initial administration, improvement was observed. Hamilton, therefore, theorized that a deficiency or a small amount of testosterone causes acne but a normal level or none at all does not; therefore, giving testosterone propionate to patients with acne should be beneficial. However, in the small number of patients he treated thus, benefit was shown only in about 50 per cent of the cases and the results as a whole were considered not to warrant treatment with androgens.

Cornbleet and Barnes²⁹ also tried testosterone therapy using 10 mg. of testosterone propionate in sesame oil. However, their results, 50 per cent

improvement, were as good with the sesame oil controls as with the hormone which was, therefore, concluded to be of no therapeutic value in acne.

The medical professions inclination to use hormones in treating acne vulgaris has gradually diminished since the introduction of the systemic antibacterial agents--in particular, the broad-spectrum antibiotics. However, a few clinicians continued to investigate the use of hormones both locally and systemically. In 1951, Whitelaw¹⁹³ treated 72 males, aged 13-18, using conjugated estrogenic substances in a nongreasy base. An amount of estrogen approximately equivalent in activity to 1.25 mg. sodium estrone sulfate was applied locally. Within 14 days a striking improvement in skin texture and tone was noted in 90 per cent of those treated. Of patients treated six months or longer, 55 per cent showed decided improvement, 21 per cent showed slight improvement, and 24 per cent failed to respond. In 23 girls, aged 13-19, who received the same treatment,

only 21 per cent responded satisfactorily and 12 per cent showed moderate improvement. There was no improvement in 67 per cent, and 26 per cent showed mild accentuation of the comedones. It appeared that in the average male topical application of estrogens to the skin of the face may either nullify the effects of excessive circulating androgens or at least decrease their influence. In the male, one third of the total circulating androgen is testicular in origin, whereas in the female it is presumably all from the adrenal glands. It is on this basis, perhaps, that the difference in results between the male and female can be best explained.

Shapiro¹⁵⁸ used 2.5 mg. Premarin estrogen cream applied topically twice a day. Over 50 per cent improved within 6 weeks. Although poorly absorbed, even if 10-20 per cent was absorbed, one is in the dosage range when given systemically, would help acne.

In 1953, Aron-Brunctiere⁵ showed that the ratio androgens plus progesterone:estrogen fits experimental findings that progesterone as well

as androgens has a stimulating effect on pilosebaceous apparatus. However large doses of gonadotrophic hormone and estrogens have a progesterone-like effect on the pilosebaceous apparatus rather than an estrogenic effect. This may explain exacerbations of acne with large doses of estrogen.

Jarrett⁸⁰ in 1955 treated 23 males and 20 females with acne with 5 mg. stilbesterol orally daily for 21 days. There was clinical improvement in 75 per cent in both sexes and no serious side effects developed. However, the acne tended to relapse after cessation of treatment. It was shown that stilbesterol causes significant decrease in surface sebum.

It has been shown that postovulatory administration of estrogenic hormones in selected patients with premenstrual acne flareups is often of distinct value. Torre and Klump¹⁸³ stated that the selection of patients is important and should include the following:

1. History of definite and regular premenstrual acne exacerbations

2. No history or evidence of 1) endometriosis 2) persistent ovarian follicle 3) cystic mastitis 4) carcinoma of the breast 5) ovarian cysts or 6) severe liver disease
3. Family history of cancer of the breast or genital organs
4. Opportunity to see the patient at frequent intervals
5. Failure to respond satisfactorily to other forms of therapy.

They preferred Premarin, 0.625 mg. up to 2.5 mg. every day for 10 days before expected menses. If the patient had any difficulty with menses, therapy should stop.

Edelstein⁴⁴ in 1960 used 25 mg. of hydrochlorothiazide daily in 109 patients having a history of premenstrual tension with acne flares. Only 10 patients failed to improve. Cornia³² used combined therapy of estrogen and chlorothiazide in 110 patients with premenstrual acne flareups, and he believes the combination superior to either drug used alone.

Petit¹³⁵ in a controlled study investigated serum gonadotrophin in treatment of acne and found no evidence that gonadotrophin benefitted the disease. Another British investigator, Jarrett⁸⁰, showed that testosterone increased the activity of sebaceous glands and aggravated the lesions of acne while progesterone in comparable doses to testosterone was without effect on sebaceous glands and did not influence acne. He also showed that stilbesterol decreased surface sebum and clinically improved the acne.

Premarin has also been given to men ages 20-39 in a dose of 2.5 mg. for 90 days by McCash and Lamar. Sperm counts were taken every 2 weeks and there was no change from the normal. There was decreased skin oiliness and clinical improvement within 28 days of their acne. However, gynecomastia developed in 11 but this gradually subsided after withdrawal of therapy.

It has been impossible to correlate the results of the many studies dealing with the therapeutic effects of estrogenic substances in acne vulgaris. This is due mainly to the

same reasons which have interfered with progress in so many other scientific and therapeutic investigations, mainly, the complete lack of standardization of experimental conditions in the various studies. The following are some of the factors which have differed widely in various studies:

A. Topical application of estrogenic substances

1. Natural, natural conjugated and synthetic substances have been used.
2. The substances have been applied in different vehicles
3. The materials have varied greatly in potency
4. The materials have been applied in different concentrations and doses for different lengths of time, and the number of applications per day has varied
5. In some studies no differentiation was made between male and female patients
6. In some studies only adolescent patients were included, while other studies

included older patients as well

B. Systemic administration of estrogenic substances

1. Natural, natural conjugated estrone, progesterone and diethylstilbestrol
2. The materials have varied tremendously in potency
3. The materials have been given for different lengths of time, sometimes by oral and sometimes by parenteral routes
4. In some studies the material has been administered steadily throughout the menstrual cycle, while in others the medication was interrupted during certain phases of the menstrual cycle
5. In some studies two different hormonal materials were given during different phases of the menstrual cycle
6. Only in a few studies were male patients included, probably because of the potential danger of estrogen administration to males.

In conclusion it can be said that the bulk of available, yet unreliable evidence speaks for the usefulness of systemically administered estrogens

in acne and does not yet support their local effectiveness on topical application. Hormonal treatment is, for the most part, obviously unwarranted. Most suitable for a trial with hormonal therapy are women in whom exacerbations occur with regularity and are distinctly associated with the menstrual period, and women who have advanced beyond the acne age but are left primarily with acne involvement of the chin and adjacent areas with or without associated menstrual exacerbations. However, for some unexplained reason, diuretics give better results than systemic estrogens.

The possible role of the thyroid in acne is quite controversial. Undoubtedly the thyroid plays a role in skin metabolism. Hypothyroidism results in a thick, wrinkled, dull and dry skin; secretion of the sebaceous glands and sweat glands is diminished. Hyperthyroidism results in a thin, soft, smooth, shiny and moist skin; sebaceous and sweat secretions are increased. Many continental workers believe hyperthyroidism is associated with acne, while Americans, especially Sutton, lay more stress on hypothyroidism. Therapeutic results

with the use of thyroid extracts are dismal.

The role of the internal secretion of the pancreas and, more specifically, the blood sugar level in acne vulgaris has long been discussed. Schwartz et al.¹⁵³ reported a series of thirty cases of acne in 50 per cent of which he found marked or borderline hyperglycemia. McGlasson¹¹³, also, maintained that acne is a condition in which hyperglycemia is an almost constant factor. However, Levin and Kahn⁹⁶, in an extensive biochemical study of acne, found no significant changes in the dextrose tolerance or in the urea, non-protein nitrogen, creatinine and calcium content of the blood. Nor could Fisher⁵¹, Greenbaum⁶², Strickler and Adams¹⁷⁶ confirm that a hyperglycemia is found in acne vulgaris.

Crawford and Swartz³³ went a step further and showed that even a high carbohydrate diet was not deleterious to ten patients with severe pustular acne. These patients were hospitalized and given daily intravenous injections of dextrose for two weeks. Fifty per cent of them definitely improved, 20 per cent showed a slight improvement, and none were worse.

Thus the problem appeared to be settled to the satisfaction of all until Wortis¹⁹⁹ noted a marked improvement in the acne of all of six psychiatric patients treated with insulin shock therapy. Improvement was noted before shock doses were reached. Wortis, therefore, suggests a sustained hypoglycemia with small doses of insulin. However, this was a false conclusion, as acne is often of psychic origin and the insulin shock served to remove concern.

Cohen²⁶ gave tolbutamide to 26 patients with severe acne who had been resistant to antibiotics and other standard acne therapy. About 80 per cent improved with this therapy. Their blood sugar levels were always within normal limits.

Singh et al.¹⁶² also gave tolbutamide to 26 patients. However, their responses varied with 20 per cent cleared and 65 per cent moderately improved.

In 1963, Grover and Arikian⁶³ showed improvement of acne by intralesional glucagon injections. They suggested that the amelioration

of acne by insulin may depend more on its effect on the cellular intermediary metabolism of glucose than on its effect on blood sugar levels. The pancreatic alpha cell hormone appears to fix to tissues in a manner similar to insulin and may possibly cause a non-specific enhancement of inflammation. However, since they punctured the acne lesions, they performed an age old proven therapy for acne lesions which is to drain their contents. There is certainly not enough evidence to support hypoglycemia for acne therapy. Results given in the above studies can be achieved by controls given placebos which only further substantiates that any acne therapy will give some results.

C. DIETARY FACTORS AND VITAMINS

Foods in general have never been held to be the sole cause of acne but they have been blamed indiscriminately as exacerbating and contributing factors in acne; this is particularly true for certain groups of foods--i.e. fats and carbohydrates. With the exception of chocolate,

fish and shellfish, the number of foods which play a specific role in aggravating acne is relatively small. It should be understood that the dietary restrictions which are so continuously placed on patients with acne are based, not on the patient's own history, which might clearly suggest that certain foods cause exacerbation, but rather on traditionally handed-down impressions that, of the various foods which may cause trouble, the ones listed are most likely to do so. Included in the list used are foods such as: chocolate, nuts, fish, shellfish, sharp cheeses, milk, oranges, tomatoes, pork products, pastries, sweet drinks, especially Coca Cola, fried foods, eggs, butter, iodized salt, and in general most fatty foods as well as carbohydrates. As a result of the diets prescribed, many patients were seen in a starving state.

The problem of sugars in the diet of acne patients has recently been re-investigated. Cornbleet and Gigli³¹ in 1961 divided 50 patients into two groups. They had approximately equal severity of acne. One group had sugar ad lib

in the diet and the other group was on restricted diet. Therapy was the same in both groups consisting of antibiotics. Observation showed no difference between the two groups with results. Glucose tolerance tests were given to 15 patients with acne and 15 patients without acne and no significant difference was observed between the two groups.

Mullins and Naylor¹²³ in 1962 reviewed the literature and found marked disagreement as to the role of carbohydrate in the diet of acne patients. They made a study using glucose tolerance tests, and they found no abnormalities of circulating glucose levels in acne patients and showed that there was no metabolic derangement of carbohydrate metabolism in the blood or skin. However, acne was aggravated by prolonged or repeated hyperglycemia because glucose provides the most favorable medium for bacterial growth. Because of the postprandial refractory period illustrated by the Exton-Rose test, the authors concluded that desserts eaten

following meals would not affect acne adversely.(i)
However, sweets such as cokes will produce sharp elevations of the blood sugar in the fasting individual. Therefore, eating sweets between meals can aggravate acne and should be sharply curtailed.

The present recommended diet for acne patients still includes restriction of chocolate, peanuts and iodized salt; however, further restrictions depend upon the individual as to what he notices aggravates his acne.

The use of vitamins has been attempted in practically every ailment known to man, and acne is no exception. That vitamin deficiencies can affect the skin is unquestioned, and the cures that can be obtained in the treatment of pellagra with the vitamin B complex is little short of miraculous. However, proof is lacking that acne is specifically due to any vitamin deficiency.

(i) This test employs a fasting blood sugar followed by a 100 gm. glucose meal and in two hours another blood sugar determination is made. Both sugar determinations should fall within normal blood sugar values. However, elevation of the two hour post prandial means hyperglycemia and warrants further studies including a glucose tolerance test.

Vitamin D was the first of the vitamins to be used in the treatment of acne. Concluding that the occasional temporary benefit observed with the use of ultra violet light was due to its action in activating the ergosterol of the skin, Doktorsky and Platte⁴⁰ theorized that vitamin D should be effective. Accordingly they administered 5000 to 6000 U.S.P. units in the form of viosterol to 35 patients. Thirty-one of the 35 showed 70 to 80 per cent improvement as judged by actual count of the pustules and the others showed 40 to 50 per cent improvement. Furthermore, exacerbations were noted in ten persons when vitamin D was discontinued.

Maynard¹¹² also reported good results with 5000 to 14,000 units of vitamin D which he believed more effective than x-ray. In a series of 132 patients, 75.6 per cent had a satisfactory result in three months. In a series of 86 patients treated with x-ray, 48 per cent had a satisfactory result in three months.

Other reports, however, were not so favorable. Henricksen and Ivy⁷² treated 210 patients

using two levels of potency, one at 20,000 to 30,000 U.S.P. units and the other at 100,000 units. Of the patients given the smaller dose, 20 per cent showed definite benefit in two to eight weeks. Of those that did not respond to the smaller doses, 30 per cent responded favorably to higher doses. This, of course, raises the question as to whether or not even larger doses might not be still more beneficial. Experimenting along this line, Wright²⁰¹ reported no therapeutic difference was observed between 100,000 and 400,000 units dosage. He further concluded that vitamin D is at times a helpful adjunct in the treatment of acne, but given alone is not curative and is beneficial only so long as the patient continues medication.

Simpson et al.¹⁶⁰ concluded vitamin D alone in doses of 5000 to 20,000 units, or combined with vitamin A, was of no practical value even as an adjunct in the treatment of acne. In their limited series of 22 patients, 45 per cent showed some improvement, but only in a few cases was the therapeutic result permanent. In 20 per cent,

the improvement was moderate or good, ten per cent of the patients became worse with the treatment and others remained the same. In no case did the results compare with the results of properly applied radiation therapy.

The rationale of vitamin D therapy for acne is not clear but some have suggested that the effect on calcium metabolism is the important factor. Calcium itself has been used. Bloom¹⁸ reported fifty per cent or more improvement in eleven of thirteen patients using five to ten cc. of a ten per cent calcium chloride solution, intravenously, every two to three days for twenty or more injections. Diasio³⁶ was of the opinion that calcium produced a rapid diminution of the edema present in individual papules and pustules but did not aid in the disappearance of comedones. However, the experience with calcium therapy is limited and until further evidence is presented it cannot be considered of much importance, nor do the reports on vitamin D warrant much optimism.

The pathology of acne vulgaris has been described as a hyperkeratosis of the pilosebaceous

follicle, similar to the hyperkeratosis occurring in vitamin A deficiency. With this in mind Straumfjord¹⁷⁰ reasoned that vitamin A should be beneficial. He reports the results of treatment of 100 patients using 100,000 units daily. Thirty-seven patients became entirely free from acne and 42 more became free except for an occasional acne papule or pustule. Benefit was usually noticed after about three months' treatment and was maximal in nine to twelve months. Straumfjord believed doses greater than 100,000 units daily were of no added benefit but possible doses less than 100,000 units would be just as beneficial.

In 1955, two separated German experiments also used vitamin A in acne therapy. Adam and Nicolowski showed that vitamin A in doses of 50,000 to 100,000 units given over long periods will decrease testicular function and hence will decrease the 17-ketosteroid excretion. Germeraad et al.⁵⁸ gave 100,000 I. U. of vitamin A three times a day to 133 patients over a 9 month period and of these 63 patients were cured or improved.

This is a very high dosage as most American workers use 50,000 units daily. They were later maintained on 50,000 I. U. daily.

The very long time required for improvement is worthy of note as it is well known that many cases undergo intermittent spontaneous remissions. Furthermore, vitamin A deficiency, which is by no means a characteristic finding in acne, results not only in a hyperkeratosis of the pilosebaceous gland, but also in an atrophy which is not the case in acne. Nor is the distribution of the cutaneous lesions occasionally seen in vitamin A deficiencies the same as in acne. In the deficiency the lesions are chiefly on the extensor surfaces of the upper and lower extremities, the shoulders and lower part of the abdomen, while in acne the lesions are found on the face, upper chest and upper back.

Lynch¹⁰² in 1940 reported that in a series of 38 patients, nicotinic acid was administered twice daily in the form of 50 mg. tablets. No other treatment was used. The results in six (16%) were classed as good, in 15 (39%) as fair,

and in 17 (45%) there was no improvement. He concluded that nicotinic acid is not a cure for acne but may be helpful, especially to reduce the seborrheic oiliness of the face. Barefoot⁸ in 1955, gave 25 mg. of nicotinic acid immediately before each meal to 19 patients whose acne had not responded to usual therapy. Ten showed improvement in 10 to 14 days. He based his therapy on the idea that nicotinic acid was an agent for counteracting iodine and bromides which may aggravate acne.

The problem of diet and vitamins as being factors in acne is not entirely solved, but current views lean towards having the acne patient have adequate foods with good nutrition. It has been shown by experiments using placebos that most any type of therapy given to acne patients will give some good results (see psychological therapy), and that vitamin therapy as stated above has not been proven to be beneficial.

D. LOCAL TREATMENT

As with other forms of acne therapy, local therapy is not without its controversies. However,

local therapy is the oldest and most widely acceptable form of therapy. Everyone who treats acne prescribes his own preference in local therapy, making an objective presentation difficult. The subject will therefore be subdivided into the major agents used; however some current products now attempt to achieve most preferred local effects in one product.

A. Cleansing Agents

In recent years a considerable number of new cleansing agents especially designed or recommended by manufacturers for acne have become available. None of them has shown a consistent and striking superiority over the previously available antiacne soaps. Thus the medicated cleansing agents such as Fostex bar and cream and those containing abrasives such as Cosmasul and Brasivol are useful in occasional cases.

Wulf and Fegeler in 1953 pointed out that disease of sebaceous glands are known to occur after contact with metals, metalloids, halogens, turpentine, lacquer, varnish, petroleum, lubricating oils, gasoline, petrolatum, tar, pitch,

benzene, dyes either by inhalation absorption, via the gastrointestinal tract, or direct contact. Soap which is a compound of fatty acids with alkali has similar effect, especially those with ethereal oils added for scenting and must be rinsed off completely. The author points out an important factor that what used to be "ordinary" toilet soaps, no longer appear to be so ordinary. At the present time, there is a trend in the soap industry to superfat previously ordinary toilet soaps. For example, Camay and Lux soap now contain cold cream, a change which may have advantages for some users but which should reduce their usefulness for the average acne patient.

Alexander and Vickers² used Brasivol with 75 cases of acne of varying severity and duration for a period of up to 9 months. Results showed 25 cases cleared completely, 37 markedly improved, and 8 failed to respond. Brasivol contains the abrasive aluminum oxide in a soap-detergent base with 1% hexachlorophane. However, the favorable results are not equalled by anyone else.

Stough et al.¹⁶⁸ used Fostex as a cleansing, anti-seborrheic, keratolytic and bacteriostatic

agent with 215 cases of acne, applying two times a day followed by rinsing. Results showed 75% improved after 4 weeks. He also used Capsebion shampoo with 300 patients with seborrhea dermatitis of the scalp. He recommended shampooing 2 - 7 times a week and 80 per cent were improved. His results are remarkable which raises the question if there were other treatments used in therapy which were not mentioned.

Another trend is to add antibacterial agents to soaps and soapless cleansers, as for example, in Dial, Lifebuoy and pHisoHex. Wexler¹⁹¹ used pHisoHex and pHisoAccream in a study of 100 acne patients. He instructed them to wash with the detergent emulsion several times a day and to apply the cream containing hexachlorophene and resorcinol every night. He obtained excellent results with 79 per cent and fair results with 15 per cent. However, it must be remembered that there is no bacteriocidal action when the preparation is immediately washed off.

B. Degreasing Agents

When excessive oiliness is present, necessitating frequent degreasing, or when washing is

not feasible as frequently as required, various other acceptable means for cleansing the face, in addition to the older degreasing agents, might be used; for example, Wash 'n Dry packets which contain premoistened throw-away tissues, or Sebanil, a cleansing solution which may be carried in a small bottle and used with cotton, tissue or handkerchief.

In 1957, Warshaw¹⁸⁷ treated 33 acne patients with "routine care" and following every washing applied 20% aqueous aluminum hydroxychloride to the entire face for three weeks to six months. Topical preparations with resorcin and without resorcin were also used. Clinical improvement was seen with 32 of the 33. The aluminum hydroxychloride seemed to accelerate initial clearing and maintain the skin in a less oily acne-free state. Other workers such as Faust and Cole and Aton et al. also used aluminum chlorhydroxy allantoinate preparations and received good results in maintaining the skin in a less oily state with resultant decrease in the acne lesions. However, these preparations achieve effective oil removal for only two hours.

C. Peeling Preparations

The pharmaceutical industry has placed a large number of "peeling" and drying preparations on the market, almost all of them based on the time-honored formulas containing resorcin and sulfur, even as they did in 1883 when Stelwagon¹⁶⁷ named sulfur the most reliable agent of that day for the treatment of acne. Since that time there has been a great variety of preparations using sulfur and resorcinol. The addition of low concentrations of hydrocortisone to resorcin and sulfur-containing products such as these does not enhance their therapeutic value.

Bluefarb et al.¹⁹ improved 873 out of 909 patients with Fostril preparations. The drying action of Fostril is due to a synergism between sulfur calamine powders and polyoxyethylene lauryl ether which is similar to resorcinol but there is no sensitization or staining of the skin. They found that hydrocortisone seemed to be especially beneficial for acne rosacea and those with marked erythema.

Blau and Kanof¹⁶ used polyoxyethelene lauryl ether alone on 420 acne patients and depending on

the frequency of application, a satisfactory, rapid and controlled drying of the skin occurred and hence acne improved in almost every case. However, 14% of the patients complained of discomfort caused by the lotion.

There has been a gratifying effort by the pharmaceutical industry to make available to acne patients both medicated and nonmedicated make-up preparations which, when applied in thin layers of skin colored material, cover acne lesions which are not conspicuously elevated above the skin surface. These preparations apparently do not contain the acnegenic properties of some of the commonly sold pancake type make-ups. There are many which are skin colored and medicated and are intended as a make-up to mask the acne lesions. Some of these are available in two or more strengths and in a variety of shades.

Horne⁷⁴ in 1961 treated 128 acne patients in a paired comparison technique using Tracne which contains resorcinol monoacetate, colloidal sulfur, and N-trichloromethylmercapto-4-cyclohexene-1, 2-dicarboximide. He found it very effective in

the older and younger acne patients because it was less drying.

D. Topical Anti-infectious and Anti-inflammatory Agents

Pustular and cystic forms of acne often require, in addition to other topical therapeutic procedures, therapy intended primarily to combat infectious and inflammatory elements. The selection and intensity of this form of therapy depends on the degree and extent of involvement. Baer and Witten⁶ state that they have tried many of the available antibiotic ointments⁵, suspensions and solutions containing tetracycline and its relatives, chloramphenicol, erythromycin, bacitracin, neomycin, polymyxin B and so forth, but they were not impressed with their efficacy in the management of pustular acne. They found the most effective of the ointments to be Quinolor Compound Ointment, but they also found that this caused contact dermatitis in some patients.

Hanfling⁶⁶ states that Triburon, a topical antimicrobial, has been very encouraging and he believes it to be more effective than bacitracin-neomycin mixtures. Berger¹³ used Cosmedicake with

with 112 women with acne and 99 out of the 112 women found the cream to be highly satisfactory therapeutically and cosmetically. The cream contains colloidal sulfur for keratolysis, salicylic acid for antiseptis, fungicidal and keratolysis, hexachlorophene for bacteriostasis and benzalkonium chloride for its germicidal effect.

Baer and Witten⁶ have used antibiotics in the management of cystic and conglobate acne lesions by local injection. For this purpose, the following mixture was prepared: The contents of a 200,000 unit vial of crystallin penicillin G (or of a 500 mg. vial of neomycin) are dissolved in 5 ml. of sterile distilled water or normal saline; to this is added 5 ml. of 2% procaine solution. When inflammation surrounds the cyst, the solution is injected around the periphery, using a small-caliber hypodermic needle, thus affording not only treatment but anesthesia to the area. The cyst is then punctured, near its edge, with a very sharp large-bore needle (no. 18) through which the contents of the cyst are aspirated; the sac is then lavaged with the prepared

penicillin or neomycin solution and some is allowed to remain in the now cleansed cyst sac. The contents of noninflamed cysts can be lavaged without injecting at the periphery. This procedure would be intolerable with the patient with many lesions. Treatment in these cases should be by systemic therapy.

E.. Relief of Irritation Produced by Peeling Agents

Steroid preparations in acne are not generally acceptable as topical therapy since they have no significant effect. However, these preparations have been shown to be very useful in relieving irritation or excessive dryness resulting from the different forms of external therapy discussed. There are many creams, lotions, and ointments available such as Aristocort Acetonide Cream, Neo-Aristocort Acetonide Ointment, Neo-Aristoderm Foam and Kenalog and Kenalog-S cream, lotion or ointment. The older preparations are Cort-Dome, Neo-Cort-Dome, Cortef and Neo-Cortef ointment. The cost of these medications is excessive and use may be prevented by careful control of topical therapy.

E. ANTIBIOTIC THERAPY

In those cases of acne which do not respond promptly to topical and other simple measures, the systemic administration of antibiotics has proved to be the method of choice. While this applies especially to pustular and cystic acne, these medicaments have proved remarkably effective in some cases of the papular form of the disease. As in all other diseases, it is of prime importance to rule out a history of known allergic sensitivity or other undesirable side effects due to antibiotic or chemotherapeutic agents before prescribing this type of therapy. There are strenuous objections voiced against prolonged administration of these antibacterial agents. Among these is the possible development of drug-resistant strains of micro-organisms and the consequent occurrence of serious infections which may prove extremely difficult to control. However, many have been using these medicaments and managed many hundreds of acne patients without encountering a single serious or irreversible side effect -

whether it be a gastrointestinal complaint, pruritis vulvae or ani, or an altered blood count.

In 1950, Evans et al.⁴⁹ investigated the normal bacterial flora of the skin and found the most common organism to be the acne bacillus, *Propionibacterium acnes* followed in decreasing numbers by *Micrococcus epidermidis*, *Micrococcus saccharolyticus*, *Staphylococcus albus*, *Monilia candidus* and *Monilia flavus*. They also noted that sebaceous glands appeared to be the major site of growth of skin bacteria but sweat glands were also significant. In 1963 Shehadeh et al.²⁰² examined the bacterial flora in 175 acne lesions including comedones, papules, pustules and cysts. Two organisms, *Corynebacterium acnes* and *Staphylococcus albus*, usually in combination occupied the various types of acne lesions. almost exclusively. The authors regarded both as contributors to the pathogenesis of acne by secondary infection.

As for the choice of antibiotic used, just about every antibiotic produced has been tried. Unfortunately the number of controlled studies

is few. Most investigators have used antibiotics in conjunction with a variety of common acne treatments already described. However, the increased effectiveness of therapy with the combined therapy cannot be overlooked.

Baer and Witten⁶ ordinarily choose to start with tetracycline combined with nystatin--compounds such as Achrostatin-V, Comycin or Mysteclin. The usual schedule is 250 mg. 4 times daily for 4 days, then 250 mg. 3 times daily for 3 days, then 250 mg. twice daily for 1 week with the dose of subsequent therapy determined by the patient's response. Using this procedure, they have kept many patients on systemic antibiotic therapy for periods from a few months to several years. They have also used penicillin by mouth in some cases. They start with at least 1,200,000 units of penicillin daily in divided doses of 250 mg. of penicillin V or potassium penicillin V, 3 to 4 times daily. The use of penicillin therapy may be the cause of the allergic reaction described with the use of antibiotics in acne.

Forbes and King⁵³ studied 567 cases of acne over a four year period and they showed that tetracycline did not lose its effectiveness when given over a long period of time. It would effectively control the acne, but did not cure it and intermittent therapy was necessary.

Robinson¹⁴¹ used penicillin, oxytetracycline, chlor-tetracycline, chloramphenicol, erythromycin and carbomycin with 391 acne patients. He found all the drugs except penicillin beneficial.

Sulzberger et al.¹⁷⁸ used the above variety of antibiotics including novobiocin and triacetyloleandomycin with 208 acne patients who were resistant to other forms of therapy. They found that most patients were improved and there were few side effects.

Hicks⁷¹ in 1961, ran a controlled double-blind study using demethylchlortetracycline (Declomycin) and placebos. Of the 30 patients receiving Declomycin, 25 had good to excellent results. Of the 16 patients given placebos, five improved favorably but 11 remained poor. He had photosensitivity and onycholysis as complications in a few cases.

Wansker¹⁸⁶ also ran a controlled study using a variety of antibiotics including tetracycline, erythromycin, triacetyloleandomycin, and novobiocin over a period of 18 months. Of the 74 patients receiving antibiotics, 74.3% improved significantly. Of the 17 patients receiving placebos, 29.4% improved as much as the antibiotic group. He found no significant difference in the drugs used.

Cornbleet³⁰ used tetracycline with 38 acne patients and 36 of them improved or cleared, but maintenance therapy was needed for over a year.

However, not all experiments with tetracycline have proved beneficial. Two British workers, Smith and Waterworth¹⁶⁴ obtained 67 specimens of material from acne lesions from 39 patients in 1961. Coryn. acnes was obtained with anaerobic cultures from 57 specimens. There was no evidence that either tetracycline (250 mg. to 1.0 gm.) or penicillin (750 mg.) penetrated into the acne lesions as there was little alteration in the bacterial flora from acne lesions after courses of chemotherapy up to 3 months.

In 1962, they ran a double blind study with 60 acne patients treated with demethylchlortetracycline, phenethicillin and placebos for one month. In each group there was improvement, the placebo group had less improvement but the difference was not statistically significant. They deduced that there was no evidence that these antibiotics made any great difference in the majority of patients.

Many investigators have used triacetyloleandomycin (TAO) in the treatment of acne beginning in 1958 up until the present. Doses have varied from 250 mg. twice a day for one to two weeks and maintenance of 250 mg. per day to 250 mg. three times a day for three days with gradual decrease to 250 mg. once a day. In general, results have shown 75% of the patients greatly improved. Most investigators showed that other standard forms of acne therapy should be included. Side reactions with the drug were very infrequent, but TAO is known to cause jaundice all too frequently with long term therapy.

When the broad-spectrum antibiotics have failed or are not well tolerated, sulfonamides have also been tried--for example, sulfisoxazole (Gantrisin), given as much as 1.0 gm. four times daily, or sulfacimethoxine (Mandribon) 0.5 gm. once or twice daily. The latter drug had the great advantage of simplicity of administration, since the dose is but one or two tablets daily. With the use of sulfonamides, a blood count and urinalysis should be done every two weeks in the beginning and, if well tolerated, every four weeks thereafter. Of course, patients are cautioned to report quickly any unusual symptoms or side effects. Many investigators have run studies with Madribon particularly and most of them showed 50 - 56% of their patients improved. Some studies were well controlled but most used combined acne therapy, which makes these studies not reliable.

Baer and Witten⁶ have found that chloramphenicol was by far the single most effective antibiotic in treating acne vulgaris. However, in view of the serious side effects on the hemopoietic system

which have been reported in very rare instances, they used this antibiotic only in exceptional cases, such as destructive forms of acne which are not controlled by other systemic antibacterial medications. Chloromycetin usually is used according to the same dosage schedule as the preparations containing tetracycline. A blood count is done weekly for the first 8 weeks and then at 2 week intervals up to and including a 4 - 6 weeks period following cessation of therapy.

F. PSYCHIATRIC THERAPY

A relatively new field of therapy of acne is psychiatric. With the advent of the new psychiatric drugs, particularly the tranquilizers, their use with acne has created many new ideas on acne therapy. In one respect, acne obviously is no different from many other dermatoses in that patients state that flare-ups of their acne are associated with particular emotional upsets or trauma. A number of studies have been done in recent years to test this claim. Since no one

has yet been able to prove the existence of direct neural regulation of the sebaceous glands and their excretory ducts, a direct action of the emotions on the sebaceous apparatus can be excluded. Robin and Kepecs⁶ have, however, shown that an increase in the quantity of ether-soluble materials occurs at the skin surface during periods of emotional strain. As has been pointed out by Sulzberger and Herrmann¹⁷⁹, this phenomenon is most reasonably explained by the fact that emotional factors stimulate sweat secretion, which, as was shown by Herrmann and his associates, brings about emulsification of fatty materials, which in turn has a definite effect on the quantity and physical state of ether-soluble materials at the skin surface. The results of Robin and Kepecs therefore do not prove that there is any direct stimulating action of emotional factors on sebaceous secretion which could account for flare-ups of acne. Another study deserving mention here is that of Lorenz⁹⁷ and his co-workers, who claim the existence of a "characteristic" emotional pattern in acne

patients consisting of episodes of anger followed by periods of remorse.

Wittkower¹⁹⁷ classed 64 patients 18 years of age or older with acne as those having rigid personalities, rebels and dreamers, overgrown children and sufferers from gross psychological upsets. They were also perfectionists, sensitive to criticism, eager to be liked and tense.

Lucas¹⁰⁰ noted the characteristics of the acne patient to include a tendency to anxiety, obsessionality and introversion, and self-consciousness. He also reported a study of a comparison between the personalities of students with acne who did not complain of it and students free from acne. When a comparison was made between students who reported psychological symptoms and those who did not, regardless of whether or not they had acne, it was found that the group who reported psychological symptoms were significantly more neurotic than the others.

Most investigators do not accept the fact that the acne patient has a characteristic psyche. Since at least 80% of the human

population at one time has acne, it is hard to accept that 80% of the population has neurotic characteristics. However, at the time of initial insult, the neurotic factors present in most individuals may become manifest; however, it would take a large series of acne patients to substantiate this and other claims of characteristic emotional factors.

MacLean¹⁰⁹ used prothipendyl (Timovan) in a small group of 25 acne patients. The drug has similar actions as chlorpromazine on the central nervous system and it also inhibits adrenalin action to the autonomic nervous system. He found 21 of the patients markedly benefitted. The patients' acne had previously failed to improve from other therapy.

Pinne has also reported good results using tranquilizers in selected patients. He states that inspection of the lesions alone should not determine the therapy. After a complete history and physical examination the patient can then be considered for type of therapy best suited for his needs. Tranquilizers are used on only those

patients who display psychiatric findings and other contributing factors for acne have been ruled out.

Unfortunately, there are not many other investigators who have reported the use of tranquilizers; however, the field of psychotherapy for acne patients is now just gradually becoming acceptable and future reports will be interesting to follow.

G. PHYSIOTHERAPY

Physiotherapy of acne has greatly decreased in importance with the advent of systemic antibiotics; however its necessity and therapeutic value still exist for certain patients. The physical agents which have been advocated for the treatment of acne include carbon dioxide slush, ultraviolet light, roentgen rays and surgical dermabrasion.

Girandea appears to be the first to use carbon dioxide snow in the treatment of acne. Karp⁶, using the technique he learned in Girandea's clinic, reported of 50 patients with

acne and post acne scars were apparently cured or much improved after four months. The technique is as follows: five ounces solid carbon dioxide is ground to powder and acetone added to form a smooth paste. To this is added one-fourth ounce of sulfur precipitate. One third of the paste is placed on a 4" x 4" gauze and brushed lightly over the acne lesions until whiteness appears. The sulfur deposit is allowed to remain twenty minutes. Erythema and slight edema appear, lasting two to three days, then disappear and are followed by a mild to severe exfoliation of epidermis. Applications are repeated at weekly intervals.

The therapeutic response is believed due to the repeated exfoliations or to passage of time. The acetone serves to dissolve the sebum, permitting penetration of the sulfur into the follicles.

Karp believed cryotherapy, as it is now called, to be of greatest value in the acne of puberty and in some cases where roentgen therapy has failed.

Dobes and Keil³⁹ reported less success than Karp but believe it of some value, especially in the papulopustular and the hard indurated forms. They further believe it is no worthy substitute for roentgen rays if such is indicated.

Hollander and Shelton¹⁵⁹ reported success in twenty-six of thirty-six patients treated with cryotherapy for post acne scars. These patients received a minimum of twenty weekly treatments. They were unable to verify the originally claimed benefits to active acne lesions since many of their patients suffered a flare-up of pustules during the course of therapy.

Friedlander⁵⁷, however, reported failure with cryotherapy in 20 patients treated for post acne scars. His patients received from 37 to 68 treatments.

Cryotherapy is no longer in vogue since better and less irritating therapies are available. Norwood¹³⁰ in 1962 is the latest to report on cryotherapy and he treated 58 patients of which 22 responded well.

With the advent of Finsen's ultra violet lamp and the development of the cold quartz ultra violet lamp in 1908 by Kromayer⁹³, suitable for dermatologic use, phototherapy as a treatment for acne enjoyed an era of popularity. Kromayer, experimenting with the new irradiations, was the first to discover that acne, among other diseases, responded to ultra violet light. After the lamp had been in clinical use for many years, Lane concluded that, although some cases do well with ultraviolet therapy, the permanency of the results are not comparable to those achieved with roentgen rays. Butler²³ however, in 1924, at the same time reported very satisfactory results and believes ultra violet irradiation is the treatment of choice with the exception of roentgen rays. However, in view of the possible dangers of roentgen rays he believes they should be used only after ultra violet rays have been tried and found wanting. He advocates large dosage, large enough to produce a dermatitis in two to three seances. He further suggests that the scalp be concurrently treated by frequent shampoo for associated seborrhea.

Ultra violet light decreased in popularity being replaced for a period of time by x-ray therapy. But currently, the use of ultra violet light has increased and especially total body exposure. The patient, if properly instructed, may be allowed to treat himself at home.

Pusey¹³⁹ appears to have been the first man to recognize the therapeutic possibilities of roentgen rays in relation to acne. In 1900, when treating a patient with hypertrichosis with roentgen rays, he noted improvement of acne which was also present. This recurred several times so he purposely tried x-ray in cases of persistent acne with good results. He advised very light dosage and discontinuation of treatment if erythema or pigmentation developed. He believed the action was to diminish the functional activity of the sebaceous glands.

Since that time various reporters have attested to the efficacy of roentgenotherapy in acne vulgaris. Hazen and Eichenlaub⁶⁸ reported treating 175 cases with only seven failures in 1921. Crutchfield³⁵ in 1923 had nine per cent

relapses, two thirds of which were cured with further treatment. Michael¹¹⁷ achieved a final cure in approximately 85% of his cases in 1928. Fox⁵⁴ in 1924 reported that of 191 patients, 111 were cured, 47 practically cured, 27 improved, two unimproved and four were recurrent. Simpson¹⁶¹ reported 500 cases with 11% failures in 1931. MacKee and Ball¹⁰⁵ published a statistical report on 5,376 cases of acne in 1934. Six hundred patients received roentgen ray treatment. Of these, 83% received satisfactory results, 12% were improved and 5% were unaffected. Smith¹⁶³ obtained satisfactory results in 89% of his patients when using 75 roentgen units for twelve or more treatments in 1942.

The early use of x-ray led to many complications because of excessive exposure. These complications were worse than the original acne and included malignancies, early skin atrophy, telangiectasia and so forth. The use of x-ray gradually declined because of its complications but also because of better therapy achieved in most cases with systemic antibiotics.

Strauss and Kligman¹⁷³ investigated the effects of x-ray to the acne patient using biopsies. They noticed that the large sebaceous glands of the human cheek are radiosensitive and their activity is moderately suppressed with 400 r. With 1200 r in fractional doses, regeneration is complete in four months. With 1500 r single dose, regeneration was complete in twelve months. They noticed that acne decreased during therapy because of sebaceous suppression but would recur following regeneration. Therefore, they recommended that radiation should be saved for the older acne patient in the age range of at least 17 - 30.

Currently, it is the belief of many that justification of x-ray therapy is lacking unless other methods have proved ineffective.

Although dermabrasion is not recognized as therapy for acne itself but therapy for post-acne scars, it will be mentioned here only in interest. Kurtin in 1953 was the first to describe the procedure and at first the procedure was widely accepted and practiced. But since its

original enthusiasm, the procedure has been declining in popularity. Physicians who do dermabrasions, and perhaps to some extent even the patients themselves, have become educated to the limitations of this therapeutic method. Consequently, greater care seems to be exercised in the selection of cases believed suitable for such therapy. Only some types of acne scarring can be sufficiently benefited by this method to warrant its use. The deep "ice-pick" type of scars and the shallow scars which produce but a mildly irregular appearance of the skin generally do not respond favorably. A detailed history must be elicited as to previous excessive x-ray therapy and any tendency to keloid scarring, hyper- or hypopigmentation or other abnormal cutaneous responses. Neurotic, psychotic, or otherwise unstable individuals with apparent fixations on their scarring comprise a large number of those who insist upon dermabrasion. Their expectations regarding final appearance so far exceed any results that can possibly be achieved by this method that they are generally

poor risks for dermabrasion. No matter what the actual degree of improvement, they are likely to be dissatisfied; and, as a matter of fact, some seem to be even more concerned about their appearance after dermabrasion than before. On the other hand, some of these psychoneurotic patients become overly enthusiastic about the results, discerning great improvement where little or none exists. Nevertheless, dermabrasion remains the best procedure for post-acne scar repair.

CONCLUSION

Current acne therapy has changed considerably in the past decade. An absolute cure, as well as the etiology of the disease, is still unknown. With modern research many new ideas have given considerable insight into the disease process and its treatment, although many treatments remain disputed.

As with any treatment the general health of the patient needs investigation. Since the acne patient is a teen-ager in most instances, one must focus his thoughts on teen-age behaviors, their many activities, their psychological conflicts. The physician cannot shrug off the problem of acne with phrases of "He'll out grow it". In a dermatosis which is caused, contributed to or otherwise influenced by as many factors as is acne, optimal therapeutic results obviously can be achieved only by attempting to correct or counteract all of the unfavorable factors, local or systemic. The current therapy and its purposes can be summarized in six basic points:

1. To remove and prevent formation of excess keratin and of follicular plugs at and in the follicular opening and in the sebaceous excretory duct. For this purpose of treatment, one has available various cleansing agents and topical applications.
2. To relieve inflammation and infection involving the pilosebaceous unit and the surrounding tissues and to prevent recurrence of such inflammation and infection. Chronic sites of infection must be eliminated. Now available and proven effective are broad spectrum antibiotics which have been given to acne patients over a period of months and years with effective control of their acne. Topical applications do not appear effective in controlling infection.
3. To decrease excessive production and delivery of sebaceous material to the skin surface and afford means for effective removal of the excess once it has reached the skin surface. Transient decrease in sebaceous material may be obtained with solvents

such as Sebanil or with estrogens which are especially effective in post-ovulatory acne exacerbations. This effect may also be achieved by x-ray but this method is not now used as frequently.

4. To avoid the external factors which frequently contribute to the development or persistence of inflammation and infection of acne lesions; squeezing, fingering, contact with wool and fur, use of greasy cosmetics, seborrhea of the scalp. This is more difficult to achieve but seems to decline with control of the lesions by other means of therapy. Relatively new in therapy is the use of tranquilizers which tend to calm the usually overly active patient.

5. To avoid or control the internal factors which frequently contribute to the development or persistence of acne lesions such as iodides, bromides, acnegenic foods, foci of infection. Diet in therapy is disputed but best results for the patient are usually found in the elimination of foods which he

observes to aggravate his acne. Foci of infection such as sinusitis, dental caries or chronic tonsillitis should be treated in their usual manner.

6. To adequately cover the lesions and thus to make the patient appear more presentable. This may be accomplished now by new cosmetic and therapeutic agents which do not aggravate present lesions or produce new acne lesions.

SUMMARY

Acne is now a controllable disease in most cases. New therapeutics have brought about remarkable results with all varieties of acne. Problems of etiology and treatment are still present but many new and still controversial reports are being made which have helped to further the understanding of the disease, hence advancing the therapy. Of special interest are the long term use of antibiotics in the combined therapy program and the use of the new tranquilizing drugs.

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