1936

Acne vulgaris with special reference to etiology and treatment

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ACNE VULGARIS: WITH SPECIAL REFERENCE TO ETIOLOGY AND TREATMENT

Presented to the Faculty of the University of Nebraska, College of Medicine as partial fulfillment of requirements for the Degree of Doctor of Medicine

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Omaha, Nebraska 1936

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INTRODUCTION

According to Darier (9) acne vulgaris is one of the most common of all skin diseases, constituting about 8.5% of all cases in the practice of dermatology. It is believed by Wise and Sulzberger (50) that the majority of the patients with acne receiving one form of treatment or another are not in the hands of specialists.

Acne in its mildest form is so common in adolescents of both sexes that its presence must be considered almost physiologic. It is probably only a small fraction of this tremendous number of acne patients comprising the especially severe or intractable cases which seek the aid of the skin specialist.

The greatest number of mild acnes are doubtless receiving the questionable benefits of advice and treatment from beauty parlors, barbers, professors of physical culture, dietitians, druggists, etc. The more severe forms of acne and those resistant to the usual therapy are fortunately comparatively rare. (50)

Acne is the easiest to diagnose, also one of the least serious as far as general health or life is concerned, however from a social point of view, it is one of the most important skin diseases for us to consider as it appears in

young people at a time when they are most conscious of their appearance. They will shun society and become bashful and morose. The presence of acne has kept many a bright and accomplished young person from securing a position or from carrying on some important or productive work.

The acne eruption is often aggrevated preceeding or following menstruation. It is most common in the years immediately preceeding sexual maturity and in early adolescence.

An attempt has been made in this brief resume to give a history of the disease with various etiological factors associated and reviewing some of the forms of therapy that have been carried out and the results obtained.

HISTORY

Greek physicians do not seem to have recognized acne, it would otherwise be strange that an affection so common and often attacking the face is not mentioned in the Hippocratic writings.

Celsus who uses the term "Varus" to denote this affection mentions remedies by which he believes the eruption may best be removed, advising turpentine, alum and honey to be mixed together and layed upon the paplues of acne.

This disease is treated more fully by Cassius (A.D. 100) and inquiring why it occurs in the prime of youth and strength supposes that the noblest and best elaborated nutritive fluids are determined to the regions affected and there stagnate and accumulate.

An accurate acquaintance with acne is shown by Galen describing it shortly under the name of "Vari" and that its papules consist of the thickened fluids of the body and that they may be cured by the use of emollient applications and purgatives.

Aetius of Amida (A.D. 543) who is well known to have collected the medical writings of his predecessors, likewise mentions that Greeks used the name "vari" to denote papules chiefly affecting the face. This is also referred to by both Paulus Aegineta and Oribasius who

was an expounder of the doctrines of Galen and of those current in his own time.

It is not again noticed in writing till the sixteenth century when Gorraeus says "Acne is a small hard papule in the face called varus by the Latins, so called because it does not itch." Sauvage adds that these tubercla are ascribed to thickness of the nutritive fluids, and that they often last until adult age and then disappear.

Plench of Vienna (A.D. 1783) appears not to have been acquainted with the acne, using only the term vari. His work was chiefly repetition of accounts by previous writers. His only original observation and statement was that vari are connected with spermatozoa and accordingly they are cured by marriage.

Erasmus Wilson makes acne to arise from a certain sluggishness of the nerves and want of activity in the skin. He believed that both the forms described by him (acne vulgaris and acne Rosacea) occur more often in women than in men. Although he admits ignorance of any internal or constitutional causes of acne, and moreover advises that the skin in these cases be excited by local stimulants, as yet does not disdain to bring now and then into play against it such remedies as blood letting and purging.

Von Hebra (1864) a great dermatologist of the time, enumerated all the causes that have been given up to this time, then disproves them. His treatment consists of inter-

nal use of cod liver oil, and the clearing of any constitutional complaints, the use of soaps and per chloride of mercury as a denudent of the cuticle, scarification of the nodules and frequent scrubbings with hot baths. (14)

In 1892 it was brought out by Jackson (17) that youth was the greatest predisposing factor in acne, that heriditary disorders of the gastro intestinal tract and sex organs had an influence. He believed the development of the sex organs and disturbances of the menses affected the digestive mechanism and in most cases acne might be properly treated by correcting the digestive disturbances.

The acne bacillus, as a possible etiologic factor, was first described by Unna in 1893 (44).

Gilchrist (12) in 1901 gives the following description of the B. Acne. "It grows slowly on glycerine agar, the colony at first being creamy white, and later turning pinkish. It grows on glucose agar, bullion, and blood serum, but not on milk. It does not decolorize with Gram's stain. It is motile and has branches but no capsule."

In 1903 MacLeod (25) and Stelwagon (40) again in 1916 admitting a parasitic agent as described go further to consider the predisposing causes with bring about the proper condition of the skin (proper soil) for parasitic invasion or prejudicial action and without which predisposing

or contributory causes the parasitic agents may in some persons at least, be found in the skin without becoming pathogenic. They believed these in certain cases distinctly etiologic such as digestive disturbances, constipation, menstrual irregularities, chlorosis, general debility, lack of tone in the muscular fibers of the skin and scrofulosis, and as outside factors anything which tends to block up the gland outlet.

It was not until 1921 that the theory was advanced by Hollander (15) that acne was caused by an endocrine imbalance brought about by the demands of puberty. This imbalance was according to him, one of thyroid activity secondary to gonad activity.

In the same year Shamberg (38) supported the statement that practically all young female patients with acne vulgaris exhibit a menstrual exacerbation of the eruption.

In 1926 MacKenna (27) wrote that at puberty the sebaceous glands in common with other glands of the body are in a state of rapid growth and frequently overactive. This over activity being the result of imbalance of the endocrine system and mentioned as other etiological factors those commonly given.

Most of the work and experimental observations since 1926 have been to prove acne vulgaris due to an endocrine imbalance.

DEFINITION

Stelwagon (39) defines acne as "An inflammatory disease, usually chronic, of the sebaceous glands of the face, face and shoulders, upper trunk, and occasionally of the back, characterizied by papules, tubercles or pustules, and sometimes nodules, or a combination of these lesions, and commonly met with between the ages of thirteen and thirty."

INCIDENCE, AGE, and RACE

Block (4) holds view that acne in its first phase is a consequence of the physiological functioning of the sexual glands analagous to that which is generally assumed for the development of the normal secondary sexual features such as the formation of terminal hair. Acne and particularly its basis the comedo appears at the time of puberty. Statistical exidence is given in support of these views based on the examination of 4,191 children in Zurich. Acne was found to attain ite maximum incidence at the age of 17 in girls and 18 in boys, the gravest cases beginning at about the age of 10 or 11 and being more serious in boys than in girls.

Cunningham and Lunsford (8) compared 2,974 young women with acne with 3,185 control students with regard to the incidence of constipation, colds and other infections, and the condition of the thyroid gland, nose and tonsils, as well as the menstrual history. There was practically no difference between the two groups in respect to incidence of these systemic disorders.

Noun (33) writes that the appearance of acne is more frequent in dark skinned people than in the lighter skinned associated with the fact that sebaceous secretions are greater in the black than in the white races, and greater among the southern Europeans than among those in

the northern part of the Continent. This is partly due to climatic conditions, but in the main may be considered as a familial and racial characteristic. It is also known that dark complexioned persons usually have larger and more actively secreting sebaceous glands than blonds.

ETIOLOGY

The following factors have been considered as having some influence on the production of acne vulgaris, however there are many other factors which have been mentioned but have been more or less ruled out due to non-support.

Ball (3) in 1922 mentioned as possible etiological factors the fact that at puberty when the functional activity of the entire body is increased the skin, which is the largest individual structure of the whole body, also participates. More especially one of the appendages of the skin, namely the sebaceous glands, which become enlarged, distended and filled with sebum. That is also the period when the mother quits scrubbing the face and neck of the children as they think they have outgrown that, and the result is they do a poor job of it. The opening of the gland becomes filled with dirt and thus we have the so called black head. The accumulated and imprisoned sebaceous material first makes the papule, and being splendid culture media, eventually becomes a pustule because of the invasion and proliferation within it of the acne bacillus and the staphlococcus albus, aureus, and citreus. This pustule may be intra or peri-glandular may be in the epidermis, the cutis vera or even invade the subcutaneous tissue. If the contents are not expressed we have sometimes the terrible

disfiguring scars and pits seen in the face which are caused by a pressure necrosis.

Ketron and Brown (19) later carried out experiments with the acne bacillus in which they attempted to infest animals by intravenous and intraperitoneal injections of the acne bacillus. Nine mice and six guinea pigs were given injections intraperitoneally, seven rabbits intraperitoneally and seven intravenously. From their experiments they concluded that:

1. "The acne bacillus is not pathogenic for mice, rabbits or guinea pigs."

2. "When introduced alive intradermally into rabbits, it produces inflammed abscesses which often persists for several months, however the same reaction occured after the injection of dead organisms."

3. "Similiar lesions follow the injection of white staphlococci, but they do not persist so long as those due to acne bacilli."

4. "In a few limited experiments in man, they were unable to find any evidence of active infection after intrafollicular injections of the bacillus although inflammatory papules and pustules were produced."

5. "Whether or not active propagation of the acne bacillus takes place in the perifollicular tissues in acne vulgaris, acneform lesions would result if the organism

was liberated into the tissues in sufficient quantities from the comedo or from sebaceous material."

Ketron's (18) more recent investigations of bacillus acnes as an etiologic agent led him to hesitate to ascribe any definite role to that organism in the etiology of the disease. Even in regard to the pustular element in acne, there is not at the present time absolute unanimity of opinion.

Most dermatologists attribute suppuration in the lesions to the staphlococcus, nevertheless there is not complete agreement about this feature of the disease.

There are some investigators who apparently regard acne vulgaris as essentially a local infectious disease of the skin based on a primary seborrhea, but the trend at present is that acne vulgaris is a syndrome in which the influence of one factor, or more likely a number of contributing factors is of fundamental importance. (30)

To regard acne vulgaris as a syndrome is more in favor at present but thus far has led to nothing tangible. At the most to rather vague generalizations clinical observations tend to indicate that certain internal factors, such as the physiologic and pathologic activities of the endocrine system and various minor disorders such as anemia, constipation and foci of infection play a more or less important role in the production of the disease. (47)

HEREDITY

Heredity has been considered by some writers as a possible factor in the etiologic background of acne. This prompted Stokes and King to run a series of 143 cases which led them to believe that familial and perhaps hereditary predisposition plays a part. They surveyed a series of 143 private records of patients with acne vulgaris and conducted a control census on 100 normal physicians and nurses with reference to the familial incidence of this disease. The last group including physicians and nurses between the ages of 18 and 27 who had never had acne vulgaris.

It appeared that acne vulgaris was twenty-six times as frequent in the parents and twice as frequent in the siblings of persons with acne vulgaris as in those of persons who have never had acne. This does not establish acne as a hereditary disorder, but it at least strongly supports the suggestion of a back-ground within the family. The question as to whether the familial back-ground of acne may not consist in exposure to the infectious agents concerned is rather opposed by the fact that parents with acne have usually recovered from the disease long before the children reach the age when acne occurs and manifests the active lesions. (42)

They concluded that the heritable factors are probably complex and do not follow a simple mendelian distribution. (42)

Contrary to this Pussy and Rattner (36) reported a case of acne occurring in one identical twin and not in the other at age 23. These twins were identical to the point of having an impacted wisdom tooth on the same side.

DIET AS A FACTOR

There is frequent reference in the literature of acne vulgaris to dearrangements of the digestive system and the mal-assimilations of food as being in causal relationship to the onset of papules and pustules. There is a very slight suggestion that food may be a cause in itself, in persons who have developed a sensitivity to those articles of diet. It has been mentioned that banannas and nuts have been known to act unfavorably upon acne, and it is a common belief in the West Indies that banannas produce acne in children whose main diet is composed of this friut. Cheese and eggs have also been alluded to as possible causes. It is well known among sailors that saltpork diet at sea is liable to produce boils and as often as not these so called boils are pustular acne. This has been attributed to the preservatives of the pork, but Wills (48) believes that the cause is pig fat. In his cases with patients whose acne, especially pustular forms and those whose spots come out in crops with intervals of freedom, has them keep diet charts. He has found as many as 25% of the cases who have shown some relation to pig fat as either the exciting cause or contributing factor. There were among them of course many cases which showed no relationship to pig fat in any form, but there were many cases where there was no report and therefore possible

that the 25% may be too small a proportion.

He concluded that if food of any kind was a contributory cause of acne, only stopping this article of diet would relieve the patient, unless the follicles were completely dried up by means of X-Ray. No lotions, pills, vaccines, or kindred treatment could be expected to arrest the process, but if the offending article of diet was determined, the omission of this was all that was necessary in the majority of cases. In some it was found that a few spots continued to evolve, but then treatment was found to have an effect which it did not produce before. These persons could take pig fat and enjoy it without the slightest sign that it did not suit them. Therefore he believed it was undoubtedly the excretion of a fat through the skin which is capable of irritation the follicular wall directly, or what is more probable, of giving the organisms in the follicles a food from which they make irritant toxins.

Willis suggests that:

1. "There are not infrequent cases of acne vulgaris and pustulata, which are dependent upon dietary factors for their onset."

2. "Only the stopping of the offending foodstuff will result in the cure of the patient or at least in permitting treatment to be effective."

3. "Very small quantities of the offending diet are sufficient to cause eruptions in very sensitive cases."

4. "The eruption of lesions may continue for a week or longer from one meal of the deleterious substance. This fact probably explains why the connection between diet and acne had not been observed more frequently."

ROLE OF THE ENDOCRINE GLANDS

There are observations in acne vulgaris which point to the circulating products of endocrine glands as being in some manner closely connected with the development of the disease. It is frequently observed that acnes exacerbate cyclically in connection with the menses and that some cases are combined with dysmenorrhea. The acnes of older women appear in a preclimacteric manner at the time when there is according to endocrinologists, not infrequently a terminal endocrine dysfunction. Pregnancy often affect the pilosebaceous apparatus and the influence of the pregnancy upon the acne dermatosis as well as upon seborrheic conditions, may sometimes be apparent. Just as acne vulgaris does not occur before the beginning of sexual activity, so also the disease does not exist in the aged.

In view of all these considerations it seems a logical conclusion that the products of the gonads and of other endocrine glands in which there is increased or altered activity at the time of puberty, of pregnancy, and of menopause, either directly or indirectly contribute to the stimulation of the pilosebaceous apparatus. This stimulus physiologically produces the beard and the secondary sexual hair and in some cases pathologically, the formation of the comedo and thus lays the foundation for acne.(15)(43)

Of especial interest at present are the recent studies of female harmone disturbances associated with acne vulgaris in which the newer methods of detecting the presence and amount of these substances in the urine have been employed.

In this country Rosenthal and Kurzroh have attempted a clarification of the problem of acne by harmone titration.

In female acne patients, in a series of 34 cases, they found normal gonadal activity the exception rather than the rule. They found estrus inducing harmones in normal amounts in only six cases and absent in twenty-seven cases and a trace in one.

These results indicate that a gonadol hypofunction, primary or secondary, does coexist, at least in females with acne. Primary ovarian hypofunction is uncommon before 20, so that it seems probable that the demonstrated hypofunction is secondary to a lack of the gonad-stimulating harmone of the pituitary. (37)

Lawrence (22) ran investigations on a series of thirty patients. A study of the urine, blood, and basal metabolic rate was made as a routine. The urine showed no significant departure from normal in any case. Mild hypochromic anemia was found in four patients, which was the only departure from a normal blood picture. Blood

cholesterol was normal in sixteen of twenty patients and slightly increased in four. The basal metabolic rate was normal in eighteen patients, between minus 10 and minus 20 in four, minus 29 in one and between plus 10 and plus 20 in five. In the latter group the increase in metabolism was not accompanied by any other signs of thyroid hyperactivity and thought to be due to emotional activites. The fasting blood sugar was normal in every patient. Dextrose tolerence tests performed on twenty-five patients showed a flat curve in fifteen, indicating increased tolerence. In five the curve indicated moderate depression of tolerence and in five the curve showed normal tolerence. From this he believed, was sufficient evidence to eliminate disturbance of thyroid function as a factor. There was no evidence sufficient to indict the parathyroids and a normal blood calcium was found in six patients. There was no evidence of adrenal disturbance and normal blood sugar values eliminated pancreatic disturbance, leaving the gonads and the pituitary as possible foci.

PATHOLOGY

"Acne is pathologically an inflammation of the sebaceous glands which may, from resulting suppurative action, mean more or less follicular destruction. The attached lanugo hair follicle is usually implicated and it is alleged by some writers that this is the primary seat of the inflammatory action or irritation. In most lesions an important step in originating the process is a blocking up of the glandular outlet either by a comedo formation, as a result of hyper-keratosis or from extraneous material; in the production of the former, atony of the muscular fibers of the skin, and especially the arrectores pili, is probably an important factor. Blocking up of the glandular outlet, however is not sufficient explanation, for it is not invariably observed and it frequently occurs without any resulting irritation or acne lesion. To this, therefore must be added as yet an unknown agent, but which may variously be microoganisms, chemical and irritation change in the secretion within the gland, or some poison or irritant eliminated by the glands,

The various conditions named in etiology prepare the soil for parasitic invasion, seborrhea holding a prominent place. As also referred to in etiology, ordinary pyogenic or similar organisms which are sometimes but not always present have been thought to be the pathologic exciting factor. A special bacillus which Gilchrist finds

has pus producing properties has been found, it is somewhat short and thick, rod-like, straight or curved and sometimes branching, and occasionally coccoid in form. Gilchrist found this bacillus in every acne pustule examined.

The inflammation begins either in or around the gland the vessels showing engorgment; in the latter event the glandular structure become secondarily involved. Inflammatory infiltration may be somewhat limited, and chiefly around the gland outlet or be peri-glandular, or it may be quite extensive and diffused and even involve several glands. Suppuration generally ensues but this is a secondary result and not necessarily constant.

The infiltration, which may be superficial or deep in the derma is inflammatory in character, with some times plasma, large fusiform, giant and mast cells and when suppuration ensues, with leucocytes added. The epithelial lining usually becomes thinned, extended and may disappear entirely when the glandular wall gives way, the lesion being then a small variably sized dermic abscess.

The contents are composed of seropurulent fluid, sebaceous matter and tissue debris. In the larger lesions not only the sebaceous gland partly or completely suffers destruction but the hair follicles as well. The character of the lesion is determined by the activity and intensity of the process; inflammatory infiltration around the gland outlet giving rise to the smaller papules, and when more

extensive and peri-glandular as well, to large indurated papules tubercles; and when suppurative action ensues to the pustule. If the suppurative action is abundant the small dermic abscess results and when intense deep seated and involving several gland, the large dermic abscesses are formed." (40)

SYMPTOMS

"The lesions occur chiefly over the face, neck, upper part of the chest and back and over the shoulders. In exceptional cases in other areas. They may be superficial or deep and consist of papules, nodules, pustules, abscesses and mild inflammatory thickening of the skin. In most cases there is associated oily seborrhea and comedones. While, as a rule, the eruptive manifestations are multiple in character some type of lesion predominates. The lesions may be few and irregularly distributed, or numerous and occupy a large portion of the areas of predilection. In most cases there are no accompanying subjective symptoms, though some of the lesions may be painful or tender. The course of the disease is chronic, showing periods of quiescence, and in mild cases the lesions may almost entirely disappear, only to be followed by periods of increased activity. In mild cases only a few lesions, chiefly papules and pustules originating in comedones continew with more or less activity for long periods of time. In more severe examples deeper pustular lesions and abscesses occur. Exceptionally several deep abscess cavities form there by producing lesions an inch or more in length which may contain a teaspoonful of pus. These often remain for a long period of time before undergoing resolution unless evacuated surgically. Comedones are usually present and most of the acne lesions develop

from these. Not all of the comedones undergo this transformation when the disorder is undergoing resolution, reddened and pigmented areas may remain for a time, while in some instances scar formation results, some of which exceptionally undergo Keloid changes." (34)

DIAGNOSIS

"The characteristic features of acne are first the manifest follicular character of the lesions and the association with comedones. Other features are its characteristic disturbances, the age of the patient and its slow course. The disease can rarely be mistaken for anything else. The two affections with which at times it may be confused are a papulopustular syphilid and variola. The clinical features of the papulopustular syphilid are sufficiently characteristic to make a positive diagnosis. The papulopustular syphilids are not so manifestly associated tieh the follicles of the skin and comedones. They are especially abundant about the nose and mouth and forehead. They tend to circinate grouping. They undergo central necrosis with a wider area of ulceration and without the central conical abscess of the acne pustule and they produce larger variola like scars. Most important of all in the diagnosis for the inexpert is the fact that the pustular syphiloderm is never confined to the acne areas, but has a wider distribution and is associated with other lesions of syphilis, especially mucous patches and general adenopathy and often condylomata. Of course the constitutional symptoms and the history are important evidences, but these may be lacking.

A discrete, mild variola may be at times difficult to distinguish from acne by the appearance of the lesions alone. The lesions of variola, however, are larger and have an aggressive, prominent character which is peculiar. They are apt to be present on the hands and of course they are of acute development. The history of the prodromal symptoms of small pox, particularly in the absence of a good vaccination mark is also of great importance in making the diagnosis." (35)

BIOCHEMICAL STUDIES

A great deal of biochemical studies have been carried out but have given little insight of the disease. Greenbaum (13) carried out investigations of tolerence to dextrose. The objects of the study were:

1. "Totry to throw additional light on the pathogenesis of acne vulgaris by means of tests for tolerence for dextrose."

2. "To determine whether or not a concealed intolerence might not explain why pustulation is so common in this disease."

Assuming that an endocrine imbalance is present in acne vulgaris the point was to determine the presence or absence of a lowered tolerence for sugar as one evidence of this imbalance.

The method persued in the study was to give each patient 1.8 grams of dextrose per kilogram of body weight dissolved in 2.5 c.c. of water. The full dose was given on an empty stomach and the specimens were drawn at once and one half, one, one and one half, and two hours after the subject received the dextrose. The specimens were examined within two hours after their removal from a vein at the elbow joint.

The definition of the test for dextrose tolerence varies, but the results in this study have been judged by

the fact that the blood sugar level in the fasting normal young adult should range between 80 and 120 mg. per hundred c.c. of blood and that after the ingestion of dextrose it should not rise above 180 mg. during the first hour and should be at or below the fasting level at the end of the second hour. The result was considered abnormal if the sugar level rose over 180 mg. or was not back to its original level at the end of two hours.

In a control group of 15 patients there were 7 or 47% with intolerence for dextrose. Of thirty-nine tolerence curves for dextrose made for as many patients with acne vulgaris there were twenty-four or 61%, that indicated a varying degree of intolerence. From the results it was decided that:

1. "If intolerence for dextrose is present in acne it is not present either in all types of acne or even in all pustular types."

2. "If there is any connection between the intake of sugar and pustular acne or if intolerence for sugar is part of an endocrine imbalance generally believed to be present in acne, this test does not appear to be of help in detecting it."

Stickler and Adams (41) used a somewhat different approach to the question of sugar metabolism in 87 cases of acne.

In all the eighty-seven determinations made by them, there were only 10% showing hyperglycemia and the conclusions drawn were "that hyperglycemia could not be said to characterize acne nor did any relation appear to exist between changes in the blood sugar and the course of the disease."

To investigate the various factors that might affect the blood sugar level and its relation to the course of acne Stickler and Adams undertook multiple determinations over periods as long as three months. They found that in numerous instances the blood sugar on a restricted diet could increase or decrease but that the patient in both instances could show clinical improvement.

Noun (33) writes that "There is no hyperglycemia present in acne vulgaris; yet empirically carbohydrates are always restricted, because it seems to be of benefit in reducing the number of new papule. Experience has shown that an excess of carbohydrate in the diet not only increases the quantity of sebaceous material and thus makes the face more oily, but that it also has a constipating effect. This may lead to the formation of fermentation products in the intestine that in turn may lead to refles irritation and an inflammation of the sebaceous glands. Iodides and bromides have an irritating

action on the sebaceous glands; as a result it is unwise for an acne patient to use medication or foods in which either of these elements might be present."

With the thought that acne vulgaris might be on the basis of hypo or hyper gastric acidity Knowles and Decker (21) and Immerman (16) sought to throw light on the etiology of the disease by means of gastric analysis but found nothing of significance.

TREATMENT

In regard to the treatment of acne it is agreed that it has not yet been satisfactoriy solved. For a time the favorable results with roentgen therapy seemed to solve the problem, but later statistics seem to show that there is still room for improvment. The more recent knowledge of female harmone physiology and therapy has stimulated a new interest in the therapy of the disease. Formerly the treatment was practically routinized with the X-ray, but at present there is a greater tendency to recognize the limitations of the lines of therapy and to individualize and select treatment according to each case.

It is evident that the treatment of patients with acne cannot be stereotyped if the best results are to be obtained. The choice of the therapeutic attack is a matter of analysis of the individual case. For the purpose of this analysis the important questions to be taken into consideration are; the information obtained by a history and systemic examination (foci of infection, anemia, diet, gastro intestinal function); the age of the patient; the mildness or severity of the case; and the endocrine factor, if determinable.

As to the first group of contributory casues (anemia, constipation, etc.), it goes without saying that they should be taken care of according to general medical

principles. The dietary regimen deserves special mention since there is no unanimity regarding the importance of diet in the disease. It is unquestionable that in individual cases diet seems to be provocative of outbreaks and in some instances the breaking of dietary instructions has been followed by relapses in seemingly cured patients.(46)

Acne vulgaris often appears as early as eight or nine years of age. Children, especially girls, should be watched between the ages of eight and twelve for an oily type of skin, with a few black heads and papules and perhaps an occasional pustule about the center of the face. If mild, these manifestations may disappear. More commonly they get worse, the follicular orifices or pores enlarge, the skin becomes sallow, the pustules increase in number, and pitted scars and bad complexion constitute a permanent damage to the skin of the adolescent. If there is no preventive control, a psychic trauma ensues, and an inferiority complex makes its appearance in many cases. From every point of view, it seems preferable to prevent and control acne, rather than to attempt to cure it after it has become well established and has done a lot of damage to the skin. Therefore, a little acne before puberty should not be neglected, as it is possible in the vast majority of cases to control it to such an extent that it is hardly noticeable and does no harm.

Preventive treatment. Scalp: If the scalp is oily, it should be washed every ten days with Castile Soap.

Face and Skin: The face and skin in these cases are usually greasy or oily. They must be made dry looking, with a slightly chapped appearance, and kept that way all the time. The treatment should be continued until at least the age of fifteen. Therefore, patience and persistence are necessary.

To make the skin dry, the face is first washed before going to bed with mild castile soap and fairly hot water; then well sopped for five minutes with lotio alba one-quarter strength and allowed to dry on the skin and remain overnight, to be washed off in the morning. This treatment should be continued until the skin is dry and rather chapped. If at any time it gets too chapped, omit the lotio alba for three days. As the skin gets used to the mild castile soap and one-quarter strength lotio alba, increase the strenght of the soap and lotion; using physicians and surgeon's soap, later tar soap, and later still green soap. Also increase the lotio alba strength to one-half, three-quarters, regular strenght; then later twice, four times and even eight times the normal strength. It is only necessary to increase these strengths of soaps or lotion if the skin does not stay dry and a little chapped. The skin

should be inspected at intervals, usually monthly, to observe the control of the dryness. In about 10 per cent of cases it may be necessary to add resorcin. In a few stubborn cases the addition of beta napthol may be found necessary to accomplish the drying of the skin. If the skin is difficult to keep chapped twenty-four hours a day, a day lotion without much visible precipitate on the skin may be used as follows: sodium Hypo sulphate ½ drachm, alcohol 1 oz., lime water 4 ounces, to be sopped on the face two or three times daily.

Patients who have a tendency toward acne are benefited by gradual exposure to the sun or artificial ultraviolet radiation. Foci of infection, constipation, unbalanced diet, bad habits of any kind, and general hygiene should receive attention.

This very simple treatment has proved remarkably effective in 47 children between the ages of 8 and 12 during the past four years. (32) (5)

Van Studdiford (45) used ovarian and orchic extracts in treating a series of patients with acne. To female patients of various ages between the periods of adolescence and the menopause, 10 grains (0.64 Gm.) of a desiccated extract of the whole ovary was administered daily. The treatment was begun five days after the cessation of menstruation and continued until the next period. Fractional doses of roentgen radiation were given at

weekly intervals.

Of 284 patients thus treated, 130 showed no improvement within eight weeks.

Because of the frequently observed curative effect of marriage on women with acne, 15 grains (0.97 Gm.) of orchic extract was given daily to each of a group of these women. The use of this extract, however, was entirely empirical, as he obtained no data on which to base a decision as to the possible substitutional or stimulating action of the extract in the production of the favorable results of this treatment.

More recently, theelin, amniotin or progynon and follutein or antuitrin S have been used along with ovarian or orchic extract, and for women sometimes independently. Van Studdiford used estrogenic substance in a substitutional role, and the luteinizing factor in a stimulative role. To this end, 3 doses of estrogenic substance of 50 rat units each were given on alternate days, beginning seven days before the calculated menstrual period. Of the 15 patients thus treated, 11 improved.

As amenorrhea seems to be a stubborn factor in the treatment of acne in women, patients with either primary or acquired amenorrhea have been of late treated by a combined method by Van Studdiford. (45) This consisted of; the administration, as a stimulative measure, of the daily injection

of 50 rat units of follutein or antuitrin S during a period of five or six days just after the time for the cessation of menstruation as calculated; as a substitutional measure, the injection of 50 rat units of estrogenic substance every other day for 3 doses, commencing seven day before the time for the next menstrual period as calculated. Of the 16 patients treated in this manner, 8 showed improvement and menstruated regularly.

Orchic extract, 15 grains (0.97 Gm.) daily, was administered by mouth to 9 young male patients with no improvement in the symptoms of acne.

The most striking observation made in this series of cases was that the males who resembled their mothers had a type of acne which persistently resisted therapy and, further, that the females who looked like their fathers had the more constant menstrual disorder accompanying persistent acne.

Women past 24 responded to ovarian therapy in a higher percentage of cases than did the younger patients.

Lawrence and Feigenbaum (23) notived that four patients who were being treated with antuitrin S for functional menorrhagia were also clearing up from acne eruptions as the menstruation became normal. One of the patients after a three month interval without treatment reappeared for further treatment. There had been a moderate increase in

the duration and amount of the periods and the acne had reappeared, with the resumption of treatment the acne vanished.

The treatment as it was carried out consisted in an initial dose of 1 c.c. of antuitrin S to determine the individual reaction to the extract. As a rule the dose was then increased to 2 c.c. three times weekly. The treatment was interrupted three to four days previous to menstrual period and resumed two to four days after menstruation ceased. In no case has there been any demonstrable effect on normal menstruation. This observation agrees essentially with those of Murphy, Shoemaker, and Rea, (31) upon the effect of antuitrin S in normal women. The fact that the acne improvement paralleled the return of menstruation to normal, suggests that the acne and the menstrual disturbance were, in these patients, both due to a similar harmonal imbalance.

The duration and amount of treatment varied with the patients. The factors determining the variation were apparently the age of the patient and the severity of the disease, but in patients of identical age and equally severe eruptions a rather wide variation of response occurred. "No explanation of this variation is yet apparent though the indications are that it depends on the gravity of the underlying imbalance, rather than on its outward manifestations.

In the majority of patients improvement has been apparent in two to four weeks and maximum benefit obtained in from twelve to sixteen weeks. Two patients gave evidence of relapse beginning four and six weeks after treatment was stopped and responded promptly to the resumption of treatment. No difference was apparent between the two sexes as regards response to treatment. Further study is needed to determine the exact nature of the imbalance."

In a series of 200 cases observed over a period of about five years by McFarland (29) in which the armamentarium of treatment used consisted of X-rays, quartz light, acne surgery, diet and hygienic measures, vaccines, bacteriophages, parenteric use of phenol, glandular therapy, and local application to the skin, his deductions were that X-ray treatment was the most valuable and effective single agent available. In mild cases he used the quartz light and believes that it is indicated in cases with a tendency to superficial pyogenic infections where an anti-bacteriocidal effect is desired.

He found acne surgery valuable in the comedone type and especially in the early course of X-ray treatment and in cases where an occasional deep seated pustule appears, the skin being otherwise normal, such pustules are often found in women at menstrual time.

The use of parenteric application of phenol has

been reported by Matusis and Pavlov (28) in which a 3% aqueous solution was used intramuscularly in doses of 1 to 2 c.c. two or three times a week. It was used on a yound man 23 years of age who had a very severe pustular indurated type on the face and neck. There were numerous pockets two to three c.m. in diameter. He had had the limit of X-ray several courses of quartz light, acne surgery, and local applications. As a therapeutic test he was given 1 to 2 c.c. of a 3% solution of phenol every third day with no other treatment. At the end of three weeks at least 75% benefit was obtained. Gradually the interval of treatment was lengthened. At the end of three months he was free from lesions and remained so. The results seem to be most striking in acne indurata but is also of benefit in milder pustular types.

General hygienic measures such as regular meals, plenty of time to eat, keeping the bowels regular, sufficient sleep, plenty of fresh air, sunshine, and exercise are probably of value but it seems questionable if a marked restriction of diet is justifiable. At least the mental make up of the patient should be evaluated before giving any drastic instructions in regard to the limitations of diet. (29)

It has been the generally accepted opinion since 1922 that vaccine therapy is of little value, though

an occasional patient with the pustular type of acne seems to respond to the treatment. Staphlococcus toxoid and bacteriophage seemingly valuable in the hands of some practioneers is ineffective in others. (11) (10) (20) (6) (29)

Following some of the earliest reports on X-ray therapy in this country, there followed a great deal of enthusiam and with the development of the technic of exact dosage the roentgen ray became the trained dermatologist's most commonly used method. So enthusiastic were the earlier reports that for years there was a general impression that little more than a proper knowledge of the use of the roentgen ray was required for the successful therapy of patients with acne. Earlier reports and impressions were that from 90 to 95% of the patients were curable in about four months. The treatment became stereotyped and aside from more or less casual directions about diet, routine correction of constipation and standard tonic regimen, when obviously indicated roentgen therapy was wholly depended upon to produce satisfactory results. (26) (51)

Amshel (1) reports a series of 169 cases using X-ray therapy with 96 or 57% cured, 53 or 31% greatly improved and 20 or 12% had relapses. Successful results were accomplished in 149 or 88% of the cases. Before starting treatment they were given instructions as to the food

to eat, the bowels were to move freely at least once each day. An attempt was made to correct menstrual disorders. Any focal infections were eliminated and local applications, or cold cream, or other greasy preparations of the skin were not permitted during the course of treatment.

One quarter skin unit was given once a week and treatments limited to ten or twelve. Of these cases 126 were females and 43 males, 19 were married and 150 were single. In no case was there hypertrichosis or scarring as a result of the roentgen ray treatment.

From these results he concluded that:

1. "Sex had no effect on the result of treatment"

2. "The response to treatment was not more favorable in married than unmarried patients"

3. "The cases which responded to treatment rapidly had a better prognosis"

4. "The mild cases were the most difficult to cure and those patients were always the most difficult to satisfy."

SUMMARY

Clinical observations tend to indicate that certain internal factors, such as the physiologic and pathologic activities of the endocrine system and various minor disorders such as anemia, constipation and foci of infection play a more or less important role in the production of the disease.

Abundant evidence exists in the literature indicating that an endocrine imbalance incident to adolescence is an important etiologic factor in acne vulgaris.

It appears that the therapy for acne will be greatly improved as studies of the glandular harmones progress. Results obtained thus far show that crude glandular therapy is far from being specific as a treatment for acne.

Recent investigation of bacillus acnes as an etiologic agent has failed to ascribe any definite role to that organism in the etiology of the disease.

The heritable factors are probably complex and do not follow a simple mendelian distribution.

There is no unanimity of opinion regarding the importance of diet in the disease.

There is no hyperglycemia present in acne vulgaris.

Gastric analysis seems to throw no light on the

subject.

Treatment is constitutional as well as local.

Roentgen ray seems to be the most certain means of eradication of the lesions.

It has been the generally accepted opinion that vaccine therapy is of little value.

Opinions are divided as to the therapeutic effects of bacteriophage.

Parenteric application of phenol seems to be of some value in treatment.

Antuitrin S has been of benefit in a number of cases.

CONCLUSION

The outstanding fact in acne vulgaris is that acne is a disease of the post adolescent age and undoubtedly closely related to change in glandular function which occur at this period. Until the disease can be approached from this angle successfully, the treatment of acne must remain the treatment of symptoms.

The fact that there is now a greater tendency to recognize the limitations of the therapeutic proceedures and to individualize and select treatment according to each case, shows that a step forward has been taken, and one that should be encouraged. It is only with a knowledge of what the present situation is that the weak points can be eliminated.

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