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ETIOLOGY and TREATMENT of ACNE VULGARIS

Glenn D. Hutchinson April 1935

Senior Thesis University of Nebraska College of Medicine

### FOREWORD

Acne Vulgaris is one of the commonest of all skin diseases. It constitutes about 8.5% of all cases in the practice of the Dermatologists. (5) Its usual onset is at the time of puberty and its incidence is slightly greater in males than in females, contrary to general belief. The importance of acne lies in the fact that is a disfiguring disease and may cause profound emotional disturbances which are not easily remedied. Young men and particularly young women who are afflicted with acne frequently suffer from attacks of melancholia, depression, and inferiority complexes. They are tremendously handicapped and may carry the scars of emotional disturbances throughout life. Therefore, in dealing with acne, it is not a skin disease of small consequence but one of considerable importance, both to the individual and to society.

# 480702

It will be of interest to review the history of Acne Vulgaris before taking up the more recent work that the work of the past may be compared with the present day developments:

Acne does not appear to have been recognized as a disease by the oldest Greek physicians. Hippocrates describes it.

Many authors believe the term varus which was once commonly used to be detrived from the Latin term varius. Celsus (25 A.D.) used this term to denote this affection.

Cassius (100 A.D.) was the first to discuss this disease to any extent. He noted its occurence in the prime of youth and strength and suggested that it was a resultant of the more nutritive materials being directed to the areas affected and there stagnating and accumulating.

In 130 A.D. Galen showed an accurate acquaintance with acne; he described it under the name vari. He believed the papules to consist of the thickened fluids of the body and that they might be cured by the use of emollient applications and purgatives.

Actus of Amido (543 A.D.) who collected the medical writings of his predecessors mentioned that the Greeks who used the name Akne to denote this disease and also vari; as papules chiefly affecting the face were referred to by Paulus aegineta and Oubasius, who was an expounder of the doctrines of Galen and those of his time.

With these exceptions there is scarcely any notice given to acne in the ancient and medieval literature. Hafenreffner and Mercurialis, whose works were specifically devoted to cutaneous diseases, make but the slightest mention of acne.

Not until the sixteenth century was it again noted in literature. Then by Gosraeus, who described it as a small hard papule of the face;

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Lorry of the seventeenth wrote to quite an extent on the changes of nomenclature it had undergone. He described methods in which it might not remain an innocent disease, but by the use of caustics indiscriminately might cause the development of cancers. He advised the use of alcoholic compounds and general local measures for the treatment. It is remarkable that after this writing Plenck of Vienna (1783 A.D.) appears not to have been acquainted with the term acne, using only the term vari. His work was chiefly the repetition of accounts by previous writers. His only original observation and statement was that vari are connected with spermatozoa and accordingly that they are cured by marriage.

In "Delineations of Cutaneous Diseases" published by Bateman in 1817 the term acne is used throughout. A classification of the disease is given and new theories as the drinking of cold water when the body is hot, in great emotional stress, etc. The treatment advised was the use of somps and other medicants that would dissolve fats. (40)

Erasmus Wilson, a well known writer of cutaneous diseases, made no attempt at description of the pathology involved. He first states that it is a resultant of sluggishness of the nerves and lack of activity of the skin. His treatment was activation of the skin by local stimulants and even venisectiona and purging. Later Wilson and many other of the writers of the times described Acne as a disease of the hair follicles and more especially of the sebaceous glands. (42)

Von Hebra (1864), who was undoubtedly the greatest authority on Dermatology in his period makes the following statement, "No one has yet succeeded in discovering the exciting causes of acne. In fact, with the

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exception of a few cutaneous irritants, which appear to work only under certain conditions, and on certain persons, we know very little of what will produce it." He enumerates all the causes that have been given up to his time and then goes into great detail to disprove them.

Von Hebras treatment consisted of internal use of codliver oil, the clearing of any constitutional complaints, the use of soap and perchloride of mercury as a denudent of the cuticle, the scarification of the nodules, and frequent scrubbings and hot baths. (40)

Jackson in 1892 said that youth was the greatest predisposing factor in acne, that hereditary disorders of the gastro-intestinal tract and sex organs had an influence. That is, 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 connecting the digestive disturbances. (13)

The Acne bacillus was brought out in 1893 by Unna as a possible causative factor. (19)

Stetwagon in 1921 summarized the current views of acne. The parasite or bacterial theory was still advanced. He believed acne to be due to a parasitic cause, not necessarily the bacillus found by Unna, the invasion of the parasite was where ever the "proper soil" was present. For the preparation of this "proper soil" he gave nine principles contributing causes. They were: Digestive disturbances which gave a reflex hyperemia to the parts affected ; constipation; menstrual irregularities; chslorosis; general debility; lack of tone of the muscle fibers of the skin; such external factors as dust, dirty environment; exposure to tar and petroleum products and such internal factors as the bromines and iodides. (34)

It was not until 1926 that any author expressed as a definite opininion that acne was the resultant of an endocrine disturbance. At that

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time Mac Kenna set forth the idea that at puberty the sebaceous glands in common with other glands of the body are in a state of rapid growth and frequently over-active. This over-activity is a result of unbalance of the endocrine system. He gave no suggestion for the control of the endocrine system and mentioned as other etiological factors those commonly given. (25)

The citation from these workers are fair examples of the accepted views of their periods. The problem's presents itself as to why some etiological factors do not manifest their disturbing influence intil the period of adolescence.

All recent investigators mention puberty as the usual onset of the disease and appear to regard menstruation with or without disturbances as an influence to the production of outbreaks of the condition.

Acne, beginning as it does at puberty in most cases, may be looked upon as the local manifestation of a general disturbance. A review of the history shows it to have been attributed to a multitude of disturbances. In the minds of many present day authors acne rests primarily upon an endocrine basis. At a time when all functions of the organism are undergoing a change from childhood to puberty; when pubic and axillary hairs appear; when the voice changes; when the breasts assume a rounded form in the female; when the thyroid enlarges; when the thymus diminushes; when gonod development appears; there is a concomitant intensification of the functions of the sebaceous glands of the skin when the changes in the body economy occur gradually and normally; when there is little or no maladjustment of that delicate endocrine balance; acne is not likely to develop. But if the balance is disturbed by intercurrent illness, constipation, anemia, improper diet or poor hygiene then the skin is likely to suffer. And these disturbances may be resultants of an endocrine disturbance just as the flushed face and the dry skin are the results of enophthalmic goiter.

An increase in the oil secretion of the sebaceous glands takes place together with a hyper keratosis of the mouths of the follicles. Thus the basis is laid for the formation of comedones. There is probably a relaxation of the perifollicular musculature, that sets the stage for the development of the comedo. All the clinical manifestations are secondary. The comedo represents a dialated follicle without an inflamatory process about it, and containing inspessated eebaceous material and enfoliated horny cells. Its black top appearing at the sufface is not due to dirt but results from oxidation.

When in some instances, the contents of the dialated hair follickes increase to an excessive amount the surrounding sebaceous glands, muscles, and other neighboring structures disappear from pressure, atrophy of the

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skin results. The follicular walls of the cystic comedo are very thin.

Usually, however, before the comedo has developed to any considerable size, it acts as a foreighn body and induces an inflamatory reaction. The plugged and distended glands are then found to have an inflammatory mantle of cells about it. The cellular infiltration varies in intensity. It accounts for the clinical papule. The follicular wall of the comedo papule is always thinner than that of the simple comedo. There is no change noted in the character of the contents. The comedo papule is thus elevated, red and free of pus.

It is not known whether the sebaceous secretion is altered in quantity, quality or both. It is known that the secretion sconer or later becomes stagnant, is held in the gland by the hyper keratosis. The ever present inhabitants of the skin surface and sebaceous glands, the pus cocci and the acne bacilli, soon find a happy medium for their proliferation and change the comedone into the pustule. The wall of the pustule under the pressure of the liquid infected contents becomes thinner and eventually bursts without an outpouring of the purulent contents. Cellulitis develops immediately below the site of the rupture and granulation tissue begins to form. The pustular abscess is the next pathological development. (32)

Contrary to the prevailing opinion amoung the laity that acne has something with lack of cleanliness, this condition bears no such stigma necessarily. The sallow complexion and the apparent dirty appearance is due to the predominance of the yellow tones in the reflected light. The dull yellow tones are caused chiefly by the excess of fat in epidermis with the cellulitis.

It is only fair to mention here that some observers believe that the acne bacillus is the primary cause of the disease. They maintain that

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this organixm causes a chemical change in the normal sebaceous secretion making it act as an irritant, and thus produces an inflammatory reaction. (14) This has been refuted and proven erroneous by Ketron and Brown. They injected intra follicularly acne bacillus and were unable to find any evidence of active infection. Others believe that alteration in the sebaceous secretion takes place first and that the organisms are secondary infaders. (6,8,11) The production of pus leads to the formation of scar tissue, for wherever there is pus tissue destruction is found. Whether this tissue destruction is superficial or deep determins the extent of the scar formation. (17) This tendency to scar formation varies in individuals. (23) Some cases with deep pustulation may show little scarring, while others with comparatively mild acne will scar to a considerable extent.

Many cases of acne tend to clear up spontaneously after the twenty-fifth year of age. Some individuals may clear up before with the establishment of normal sexual relations. This tendency to spontaneous involution would seem to carry weight to the theory of endocrine unbalance as the cause of acne. Normal sexual activity by speeding up certain metabolic functions, probably hastens the establishment of the endocrine balance and gonad development. On the other hand, many cases of acne do not improve after marriage, not even as late as the thirtieth year. These may be instances of over-stimulation, thus throwing the mechanism out of balance or the abnormal processes may have continued so long that the capacity for proper interplay of the balancing forces is exhausted, or other causes of derangement supervene.

There are also many cases of acne occuring for the first time in women in their late twenties or thirties. These are often associated definitely with menstrual abnormalities as is evidences by the improvement in some them under glandular therapy. (39) Hollander collected a series of

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cases of acne in persons between thirty and forty two years of age. In every case the social status could be classes as unmarried or widow. The question arises as to whether or not the pelvic irritation caused by stagnation in the reproductive organs is sufficient to produce a hyper-stimulation of the sebaceous and pilosebaceous glands to abnormal activity without the involving of the endocrine system. (10) Rosenthall and Kurzrok in a series of thirty-four cases of acne in women found no ovarian hormone estrine in twenty-eight, greatly diminished in one; and very near normal in six. (31)

Van Studdiford who used the hormones of sex glands in the treatment of acne found that the use of testicular extract for males was an absolute failure and only a 45% success in females using dessicated ovarian extract. These results in some three hundred cases would tend to give whight to the disproving of the endocrine theory as the active etiological factor in acne. However, Van Studdiford went further with his work. To young girls he gave dessicated testicular extracts and to young boys dessicated ovarian extractt with the result of about a 75% cured or markedly improved. In cases where estogenic hormone alone was used or used in conjunction with antuitun or folliculin the same percentage of success was had. He also had excellent results with cases that had had double orphexectomy as young individuals. (47) These results follow closely the results of Rosenthall and Kurzrok.

Lane of Boston reports success with amniotin. However, in his case the acne reoccurred on discontinuing the amniotin. (17)

Bruno Black looks upon comedone formation in acne as a physiologic manifestation of the organize at the time of puberty. He divides zere acne into faux two phases; first, that of comedone formation, and second, an inflammatory and suppurative process on the basis of infection. Block attempted to ascertain exactly when and how often acne makes its appearance, and what

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relation it bears to puberty, especially to the appearance of secondary sex characters such as puble and axillary hairs and menstruation. His figures are extremely interesting and almost startling. He examined 2,136 girls between the ages of 6 and 19. Those who had acne ranging in severity from the presence of a few comedones to numerous papules and pustules, were 1,273 or 59.6% of the girls and 1408 or 68.5% of the boys. If the cases having only a few comedones were not counted , 8% of the females and 20% of the males had true acne, or 14% of 4,191 cases. In other words every twelfth girl and every fifth boy in his series had true acne. He correlated the cases of acne with the presence of axillary or puble hair or menses and found that a greater number of cases ofcurred when these secondary sex characters were present than when they were not present. (1) It is easy to conceive of Block's idea of acne as a physiological manifestation of the organism on the basis of gonadal control as the hyper-pigmentation of the female in pregnancy, for pregnancy is a physiological process.

In an attempt to determine the hereditary and familiar background of acne Stokes and King analyzed 143 cases of acne vulgaris and 100 controls. They found that acne is 26 times as frequent in the parents, and twice as frequent in the offspring of persons with acne, as in those persons who hve never had acne. They were careful to point out that this does not establish as an hereditary disorder but that it supports the suggestion of a background within the family. It is their impression that the pyogenic complication of acne or the tendency to pyogenic infection is the important familial tendency. (36)

Van Studdiford found that the majority of the females with acne resembled the paternal parentage and the males the maternal. (39)

Pussey and Roultner report a case of identical twins one with acne and one without. This is out of accord with the above general beliefs that

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that heredity plays a part. However there are always exceptions. (30)

Consider some of the conditions which may aggravate acne or change the comedone phase into the pustular phase. These are constipation, secondary anemia, high carbohydrate diet, foci of infection and poor skin hygiene. These timeworn ideas have been given **taxmagh** too much etiological significance in the past. While they may be of considerable**f** importance in making acne worse, they do not appear to be of primary etiological importance. Constipation, anemia, focal infection, and improper diet have their place in lowering the patient's resistance to infection. Too much carbohydrate in the diet, for example, may work harmful effects in either of two ways: by furnishing an enriched curture medium for the growth of organisms (36) or by favoring fermentation in the intestinal tract. (29)

Many studies have been made on sugar metabolism in acne. These have been chiefly to determination of the sugar content in the blood. Schwartz in 1916 was the first to report hyper glycemia in acne vulgaris (33). Wilson and McGlasson (43) also made simular reports.(22) Greenbaum did not find this to be true.(9) Stickler and Adams found about 15% of acne patients exhibited hyperglycemia, but since a fair percentage of normal individuals at times also show hyperglycemia they concluded that acne vulgaris is not characterized by an increase in blood sugar. They also found that changes in blood sugar in individual cases over three months did not coincide with clinical changes for better or for wørse. (35)

The high content of cholesteral and its ethers as well as the other sterols in the normal skin secretion makes its variations an interesting subject as a possible predisposing factor in certain dermitosis. The fact that cholesterol plays a prominent part in typhoid defense, its ability to protect blood cells from a hemolysis and universal presence of cholesterol or related sterols in plant and animal cells may lead one to suspect choles-

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terol has a prominent part in etiology or course of acne vulgaris in which the skin secretes an excessive amount of sebum. Stickler and Adams studied the cholesterol content of the blood in an effort to determine whether there is any relationship between the cholesterol of the blood and skin diseases with special reference to acne, and where there is any variation during the course of the disease. They found in a series of 103 dases that hyper cholesterinnia is not characteristic of acne vulgaris and the cholesterol content of the blood does not follow variations of acne vulgaris. (35)

Calcium has been thought to play an active part in acne in as much as it is a factor in the mechanism of the Autonomic nervous system which controls the glands of secretion. This is based on results from extensive studies which have favored the importance of calcium in relationship to the autonomic nervous system. The equilibrium between the potassium and calcium ions around and in the cell without which the cell would not function normally, is established by the autonomic nervous system. But it is also true that the action of the autonomic nervous system is dependent upon the ions themselves, for an increase in the potassium produces the effect of vague stimulation; increase in the calcium ions the effect of stimulation of the sympathetic nerves. On this basis some have tried with some success the use of calcium chloride in the treatment of acne. Bloom reported success in 13 cases. (2) On the other hand Levine and Kahn showed that the calcium content of the blood was not decreased in acne. (18)

In some cases gastro-intestinal disturbances may be found. With the thought that acne vulgaris might be on the basis of hypo or hyper gastric acidity, Immerman ran a series of cases and found no correlation and no retention of the gastric contents. (12)

Constipation and flatulence are the usual symptoms. Cunningham and Lunsford, in a study of 2,974 cases of acne in women at the University of

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California found that 246 or 9.6% complained of constipation. In a control series of 3,170 cases in which acne was not present, constipation was listed in 298 or 9.4%. Constipation, therefore, when present may be considered as merely an incidental factor in acne. (4)

Schwartz found in 60 cases of severe acne that 11 or 18% showed no evidence of protein putrefaction or carbohydrate fermentation; 22 or 36% showed protein putrefaction; 27 or 45% showed carbyhydrate fermentation in stool examinations. It would seem, therefore, that while a patient may or may not be constipated, intestinal indigestion may still be present. (33)

Improper skin hygiene is another factor which may aggravate some cases of acne. The use of the wash cloth, the application of greases and creams, and picking at lesions. All are to be condemned. The washcloth frequently becomes the inoculating agent for pus organisms from one portion of the face and skin to another as pustules are ruptured during its use. Greases and creams, besides being excellent culture media for organisms, assist in blocking the mouths of the sebaceous glands and thus help the increase of comedone formation. The tendency of acne patients to pick and squeeze pustules and comedones should be discouraged as it is usually done in an insanitary and unskillful way. The improper expression of comedones and pustules causes an increase in scarring and favors infection.

From present knowledge there does not seem to be any way of preventing an individual from acquiring acne vulgaris. Eunuchs are said never to have acne. (40) But as prophylactic measures we cannot make eunuchs of all the boys and girls. Further development in endocrinology is necessary for the control and treatment of acne. For the present, utilization sfx to the fullest extent of the modern methods of conventional dermatological treatment must be made. Bearing in mind that acne is due to a disturbance in the sebaceous gland activity of the skin, the treatment may be divided into

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constitutional and local treatment. To secure the best results a combination of both should be used.

Common sense should be the guide in determining the diet. Text-book methods should not be too closely followed as each case must be studied as an individual problem. In general, all measures should be taken to improve the patient's general dondition and resistance to infection. Foci of infection should be removed, constipation should be corrected, anemia (37) combatted and intestinal fermentation corrected by a suitable diet. If there are menstrual or other manifest endocrine disturbances, an attempt should be made to rectify them.

In the local treatment of acne, sulphur, resorcin, and salicylic acid in the form of lotions and ointments have been used for many years. These substances cause exfoliation of the skin and exert a more or less antiseptic action. (28,7) Some cases of acne can be cleared up by the judicious use of these agents, but their action on the whole is uncertain and time-consuming. (41)

Vaccine therapy has had enthusiastic supporters, but is chiefly useful in some cases of the deep pustular type of acne. Vaccines have no effect on the comedones or on the activity of the sebaceous glands, but they may be used as an adjuvant to other treatment in selected cases. (16,8)

In a reference above the calcium treatment was reported by Bloom. (2) (6) No report has yet appeared as to the lasting effect of this form of treatment.

Martusis and Pavlov, also MacFarland treated a number of cases with pareteric phenol, a 3% aqueous solution with success in three months. (21,24) Again, this has not been checked as to the lasting effect.

Ultra violet radiation frequently will produce an improvement in acne, buts its action is merely temporary and recurs as a rule. Rapid, temporary improvement may be obtained by producing severe reaction followed

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desquamation. Some types of acne, however, get worse under such therapy.

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Mone of the methods of treatment so far mentioned can be compared with the results produced by superficial x@ray therapy in acne following MacKies method. (23,3,20)

X-rays areused in acne because they inhibit glandular activity and aid in the absorption of infiltrated areas. It is known that the most active cells are most susceptible to radiation. The actively secreting cells of the sebaceous glands are sometimes stimulated to greater activity by the first few **MARSER** doses of x-ray, but later their activity is inhibited. Symphocylic cells, which comprise most infiltrations, because of their radiosensitivity are disintegrated and become absorbed. (8)

When the hyperactive glandular elements of the skin are inhibited and the hyper-keratosis corrected, the comedones and papules gradually disappear, the skin becomes less oily and acne is cured. This happens in about 90% of the cases treated. In about 5 to 10% reoccurrences of a few papules or comedones are noted, but these are usually relieved by a few extréa treatments. (26,11,3)

There is considerable discussion as to whether  $x \oplus ray$  increases scarring in acne. Recently Niles in a study directed towards this question gave 40 patients an average of  $12\frac{1}{2}$  weekly exposures of one-quarter of a skin unit to one side of the face, and no x-rays to the other side. He found that the scars were equal on both sides in 32 of the cases, more pronounced on the untreated side in 5, and greater on the treated side in 3. (27) He concluded that the amount of scarring after acne was directly dependent on the severity and duration of the disease and tendency of the patient's skin toward scar formation. The x-ray seems to have no influence on this tendency. Other authors have corroborated this work. (28) The sconer the effective treatment of acne is started the less the scarring effect.

#### CONCLUSION

It appears that Acne Vulgaris is far from having its active etiology worked out.

Concurrent clinical experience furnishes certain definite data concerning the predisposing cause of this affection and certain factors which provoke out-breaks, but no one has made an atorized pronouncement on the complex etiological relationships.

Although insufficient proof is yet at hand, recent work shows that the gonodal endocrine system and especially the estrin hormone or some constituent of it has some definite place in the basic activating cause.

Sugar tolerance and cholester 1 content of the blood play no part in acne.

The staphlococcus, streptococcus and Unma's acne bacillus are only adjunct factors.

That any condition that lowers the constitution of the susceptible individual is an aid to the disease but not the active cause.

Treatment should consist of constitutional and local methods. The administration of compounds containing estrin are of value. The use of Phenol and calcium chloride are also of definite value. The only definitely proven treatment at present is the X-Ray. In Taddition X-Ray does not cause worse scarring. On making a summation of all the material presented here, we find that the work at present is far too inadequate to either treat definitely or give active etiological cause in order that prophylactic action may be taken.

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