

Pantothenic Acid in the Treatment of Acne Vulgaris "A Medical Hypothesis"

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The Pathogenesis of Acne Vulgaris: A Medical Hypothesis

Over the years the pathogenesis of acne vulgaris has been extensively studied including, the structure and function of the pilosebaceous follicle, the physiology of sebum, microflora in acne vulgaris, and abnormal follicular keratinization, considered to be one of the earliest events in acne formation. Despite the concerted effort of many scientists, internists, pathologists and dermatologists, the pathogenesis of acne vulgaris remains largely elusive.

In this paper, I would like to approach this problem from a different perspective. My clinical observations suggest that acne vulgaris may be closely related to the consumption of diets, which are rich in fat content. This impression is by no means novel. Textbooks do briefly mention this correlation though, more often than not, it is dismissed as irrelevant. However, my observations have led to quite the contrary conclusions. Not only is the fat content of food closely related to acne vulgaris but it forms some sort of linear relationship with the disease process. The more fat the patient consumes, the more severe will be the acne process. This observation is in line with the opinion of many dermatologists that chocolate, which is composed mainly of the creamy part of milk, and has a high degree of fat content, is bad for acne. Significantly, in this group of patients, any deliberate attempt in trying to avoid a fatty diet over a period of weeks, if not days, will often result in important compound, cholesterol, which in turn is basically synthesized from units of acetyl-CoA. In the synthetic process, the body naturally is always trying not only to reach for a normal level of androgens, but an optimal level, so as to allow the body to function at its best. However, this is not always possible, and the normal level reached may not represent the optimal level. This is nature's flexible way of dealing with shortage of essential dietary elements in any form to achieve a level that is just enough to manage the present situation, leaving a variable degree of shortage from the optimal level. In the present instance, in the two groups of boys, one group may have a normal level of androgens that is falling short of the optimum. One possible explanation

for this is that there is a lack of basic building blocks, the acetyl-CoAs, which deter the body from operating at peak efficiency. If this is a viable possibility, it suggests that a plentiful supply or a deficiency of acetyl-CoA in the body may play a role in the acne process. This is certainly possible. Aside from its role in the synthesis of the sex hormones, acetyl-CoA, of which Coenzyme-A is the important component, it is also important in fatty acid metabolism as an acyl carrier in the lengthening and degradation of long chain fatty acids by adding or removing acyl groups in the metabolic process.

Acne vulgaris is related to lipid metabolism as well as the sex hormones, both of which have a lot to do with Coenzyme-A. This relationship provides a reasonable ground to link up the acne process to Coenzyme-A and to investigate the pathogenesis of acne vulgaris along this line.

The Importance of Coenzyme-A

In trying to link acne vulgaris to Coenzyme-A, it is important to have a hypothesis supporting some basic facts. A closer look at Coenzyme-A may provide the evidence.

A Sharing scenario; As a coenzyme active in both fatty acid metabolism and sex hormone synthesis, Coenzyme-A is shared between two different metabolic processes. This is not uncommon in biochemical reactions in metabolism, where a coenzyme is often shared among a number of reactions. Coenzyme-A is arguably the most important coenzyme in the body, and when a coenzyme is involved in the metabolic process to such an extent as this, it becomes legitimate to ask if a shortage and deficiency is possible. To answer this, a brief look at the structure of Coenzyme-A is warranted.

Coenzyme-A is formed from adenosine triphosphate, cysteine, and pantothenic acid. Of these pantothenic acid is the only component that is a vitamin, and must be provided from our dietary intake. Could there be an insufficient intake of pantothenic acid resulting in a deficiency in Coenzyme-A, which would leave the body unable to cope with all the reactions, that it has to perform with that all-important coenzyme? Conventional wisdom does not think so. It is suggested that pantothenic acid, being ubiquitous, can be had from whatever kind of food that is taken in, and that there is no question as to its deficiency in our body. However, a deficiency is still possible. After all, when so many reactions are dependent on the same agent, its demand must be tremendous. Shortage under such circumstances is not entirely impossible.

The Crucial Question and the New Theory

If the question of deficiency of Coenzyme-A does come up, how does it affect acne, knowing its importance in fatty acid metabolism and sex hormone synthesis? This is the crucial question. This is where the new hypothesis on the pathogenesis of acne vulgaris is based, and this is where it diverges from conventional medical ideas. The author's proposed hypothesis for the pathogenesis of acne vulgaris is that the disease process is not caused by androgens, or any other sex hormones, but rather, the disease process results from a defect in lipid metabolism that is secondary to a deficiency in pantothenic

acid, hence Coenzyme-A. Coenzyme-A, in carrying out its function efficiently both as an agent in fatty acid metabolism and an agent in androgen and sex hormone synthesis, has to be present in sufficient amounts, and anything less than sufficient will result in some compromise.

Mother Nature's Choice

Faced with the dilemma of a shortage of Coenzyme-A the body will tend to make a choice that is to the best advantage of the individual. The body does so by largely maintaining the functionally more important reaction, while at the same time slowing down the lesser important one. The choice here is a relatively simple one. Nature will seek to take care of the synthesis of hormones first, because continuation of the species depends on the development of the sex organs. Fatty acid metabolism is, for the time being, at least in part halted. Lipids start to accumulate in the sebaceous glands, sebum excretion is increased, and acne begins to appear. When there is enough Coenzyme-A in the body, however, both reactions will be well taken care of. There are enough sex hormones for the sex organs to develop. The lipids in the sebaceous glands are completely metabolized by sufficient Coenzyme-A, and there will be no unwanted lipid in the glands and little sebum will be excreted to cause acne vulgaris.

The Mystery Revealed

The mechanism proposed above may be the reason why two groups of adolescent boys both with a normal blood level of androgen may exhibit differences in the incidence of acne. The group with acne is the one that has not enough pantothenic acid in the body, whereas in the other group, pantothenic acid levels are not deficient.

This new theory seems to work well here, and can be tested in other metabolic situations. In the case in which endogenous androgen stimulates acne, whereas exogenous does not, the reasoning for the observation is the same. Any endogenous androgen synthesis will require the participation of extra amount of pantothenic acid. This will channel off some of those that are doing the work of fatty acid metabolism. Consequently, fatty acid metabolism becomes less efficient and the individual is more prone to have acne.

Today, the percentage of adult women that have acne is increasing. Some of these women may not have had acne as teenagers, and are surprised to find that they have to deal with this unpleasant problem during their adult years. Acne can have profound psychological and social effects on adults, just as it does in teenagers.

Many women in their 30s and 40s experience high levels of life stress because they shoulder the multiple burdens of career, child rearing, and housework, and often the responsibility of caring for their own aging parents. Perhaps this increasing level of stress has contributed to the rising incidence of acne in adult women.

Microcomedo

Acne vulgaris of adulthood is similar to teenage acne. The pilosebaceous units of the face, chest, and back can be involved. The primary lesion of acne is the "microcomedo." A microscopic plug develops due to the presence of thickened and impacted keratin (dead cells) and excess oil production (sebum). More and more of the keratin and sebum back up behind this plug and form a distended follicular pore. This results in either an open comedo (blackhead) or a closed comedo (whitehead). The enlarged pilosebaceous structure allows *Propionibacterium acne's*, an anaerobic diphtheroid, to proliferate. *Propionibacterium acne's* contributes to the breakdown of lipids to free fatty acids, which are highly inflammatory. The distended follicle can rupture, causing further inflammation and the development of papules, pustules and nodules.

Acne Rosacea

Another skin disease that simulates and can coexist with acne vulgaris is acne rosacea. This skin problem is common in women, most often between the ages of 30 and 50. The face, especially the middle third, is erythematous and flushed. Multiple telangiectasias are frequently present. Small papules and pustules, which may look similar to those seen in acne vulgaris, are common, but the microcomedo component of acne vulgaris is absent in blepharitis. Rosacea keratitis is less common, but potentially vision-threatening. Rosacea is another skin disorder that is frequently stress related.

What about premenstrual flare? In the luteal phase of the menstrual cycle, progesterone is secreted abundantly by the corpus luteum. This naturally will take up a lot of pantothenic acid from the body's pantothenic pool leading to a re-distribution of the vitamin and putting enormous pressure on fatty acid metabolism. When this metabolic process is not performing satisfactorily, lipid begins to accumulate in the sebaceous glands, an increase in sebum is excreted, and acne follows. That is why even though progesterone has no effect on sebaceous gland activity, an increasing level of progesterone in the late stage of the luteal phase leaves the acne patient with a prominent flare.

Similarly, this may explain why eunuchs rarely exhibit acne. Since so few sex hormones are secreted, the pantothenic acid pool can deploy a more significant portion of its reserve to metabolize fatty acids. When this is efficiently done, little sebum is excreted, and no acne is formed.

This theory also explains the paradoxical problem of equal sex hormones that counts. Both males and females need sex hormones for the development of sex organs and the secondary sexual characteristics. The only difference is that in the male, the female sex hormones predominate. Apparently the synthesis of sex hormones uses a large portion of the pantothenic acid pool, leaving a relative shortage of it to efficiently metabolize fatty acids. The result is that acne starts to erupt, at the same time the sex organs begin to develop at puberty.

The reason acne first erupts at puberty is not, therefore, endocrinological, but rather secondary to the deployment of a substantial amount of pantothenic acid for the purposes

of synthesis of sex hormones, leaving a relative deficiency for fatty acid metabolism. The size of this pantothenic acid pool and the ability with which the individual can deploy reserves from the pool varies and is likely to be influenced by genetic and dietary factors.

In conditions in which there is an increase in secretion of any hormone whose synthesis requires the participation of pantothenic acid, acne may erupt. This is frequently seen with those hormone secreting tumours of the ovary, testis and the adrenals. The rapid decline in incidence of acne after adolescence can also be explained. After the sex organs are fully developed, less sex hormones are required, leaving an adequate supply of pantothenic acid to serve the function of fatty acid metabolism. When this function is efficiently accomplished, sebum secretion dries up, and acne starts to fade.

Deficiency in Lipid Metabolism

In linking the pathogenesis of acne vulgaris to a deficiency in lipid metabolism and pantothenic acid, it is worthwhile to remember that fatty acid metabolism is not the sole domain of pantothenic acid. There are some other essential dietary factors that are also of importance in the same process. Together they form a system that will make the whole metabolic process as efficient as possible. Preliminary studies by the author suggest that, together with pantothenic acid, biotin as well as nicotinamide help to further improve the therapeutic results. By themselves alone, they are far less effective in helping acne patients than with pantothenic acid, and this serves to support the suggestion that pantothenic acid plays a central role in lipid metabolism. Lipid metabolism is a complicated process, and is often intertwined with other metabolic processes, sharing with them common coenzymes in widely different reactions. When there is an increase in level of some of these coenzymes, there may be a shift in the directions of some ongoing reactions, and may affect lipid metabolism as a result. This can manifest clinically as acne vulgaris. To illustrate this, there are reports showing that acne may be induced by administration of large doses of vitamin B12 alone or in combination with B6. Cessation of the administration of these vitamins will bring a halt to the acne eruptions. If the body is in a relative deficiency state in B6 and B12, administration of the vitamins will enhance the reactions that involve the participation of these vitamins. This will set up a chain of events, some of which entail the participation of pantothenic acid. With the total pantothenic acid pool fixed relative to an increase in other vitamins, emphasis of any reaction involving pantothenic acid will automatically mean a cutting back on other reactions that require it as a coenzyme. This will often include those involving lipid metabolism, resulting in a certain degree of deficiency in that metabolic process, hence the increased incidence of acne vulgaris in these studies.

Stress Related Acne

It is perhaps relevant here to consider stress as another common factor that is known to affect acne adversely. Stress in many forms poses as an aggravating factor in acne lesions. Lack of sleep at night, pre-examination tension, any psychological problem that may worry the patient will bring on new acne lesions. To understand this, one should recall that in combating stress, the body will secrete glucocorticoids from the adrenal

glands as a means to adapt to stress, what is commonly known as the fight-or-flight reaction. The glucocorticoids, like the sex hormones, are derivatives of cholesterol, and increased demand for this hormone will draw on the pantothenic acid pool. Lipid metabolism may therefore be compromised, rendering the body more prone to acne.

If pantothenic acid deficiency is indeed the main causative agent in the pathogenesis of acne vulgaris, it is logical to ask how much pantotheic acid patients are lacking in absolute amounts.

Deficiency Syndromes

Nutritional requirements can rarely be met through a well balanced diet, and dietary supplements, including vitamins, are often required. It is the generally held belief of the medical profession that vitamins, though essential to life and not synthesized in the body, are not required in great amounts. This view was challenged, notably by Linus Pauling. In his book, *How to Live Longer and Feel Better*, Pauling provided vigorous proof, through comparative studies in animals and from an evolutionary point of view, that vitamin C supplements are needed if an optimal state of health is to be achieved. Not only is supplementation necessary, but the amount required is far greater than most people believe, as with the case of vitamin C where the optimal dose may be 10 or more grams a day. This issue was a point of heated debate in the 1970s and 1980s.

Though Pauling has quite a large following, by and large, the issue was dismissed by the mainstream medical profession, because of a lack of theoretical support and a general bias against nutritional and vitamin therapy. But, in view of the new evidence suggested in these and many other papers, it seems appropriate that the issue be considered.

How Much Pantothenic Acid?

In trying to determine the amount of pantothenic acid necessary to relieve acne patients of their symptoms, Pauling's experience with vitamin C provides a good guideline. Pauling had for a long time recommended vitamin C in high dosages to achieve optimal health. Radically different from what is recommended by the Food and Nutrition Board of the National Research Council (who recommended 60 mg daily). Pauling's recommended daily intake of vitamin C amounts to several grams a day. The recommendation was stepped up to 15-20 grams a day in his later years. Using these recommendations as a background, it becomes somewhat easier to arrive at a proper dosage for pantothenic acid in the treatment of acne vulgaris.

Pantothenic acid, which acquires its name from the Greek word meaning ubiquitous, is present in all tissues. Its universal presence is an indication of its importance. This is further reflected by the many reactions that it catalyzes. It should not come as a surprise then, that the amount of pantothenic acid required for optimal health, is of the same order of that of vitamin C. Based on this argument, the dose of pantothenic acid administered to the acne patients was up to 10 grams a day, and the result of these studies were first reported in *Medical Hypotheses*.

The Effect of Pantothenic Acid on Acne Vulgaris

One hundred patients of Chinese descent were included in the study, 45 males and 55 females. The age ranged from 10 to 30, and with about 80% between 13 and 23. The severity of the disease process varied. They were given 10 grams of pantothenic acid a day in four divided doses. To enhance the effect, the patients were also asked to apply a cream consisting of 20% by weight of pantothenic acid to the affected area, four to six times a day. With this treatment regimen, the response is as prompt as it is impressive. There is a noticeable decrease in sebum secretion on the face usually 2-3 days after initiation of therapy. The face becomes less oily. After two weeks, existing lesions start to regress while the rate of eruption of new acne lesions begins to slow down. In cases with moderate severity, the condition is normally in complete control in about eight weeks, with most of the lesions gone and new lesions only to erupt occasionally. In those patients with severe acne lesions, complete control may take months, sometimes up to six months or longer. In some of these cases, in order to get a more immediate response, it may even be necessary to step up the dose to 15-20 grams a day. In any event, the improvement is normally a gradual and steady process, with perhaps minor interruptions by premenstrual flare or excessive intakes of oily food. With this form of treatment, another striking feature is the size of the facial skin pore.

The pore size becomes noticeably smaller within one to two weeks, very often much sooner. Like sebum excretion, the pores will continue to shrink until the skin becomes much finer, giving the patient a much more beautiful skin.

This decrease in skin pore size is presumably related to sebum excretion. When an acne lesion is formed, there is in the epithelial cell of the hair follicle an accumulation of lipids, leaving the epithelial cells bulky and the lumen of the gland narrowed. When there is a concomitant increase in sebum flow, the follicle has no choice but to hypertrophy to accommodate the changes, resulting in an enlarged skin pore and coarse skin. With the administration of pantothenic acid, the whole process is reversed. Lipid metabolism becomes normal and efficient. The epithelium is no longer laden with fat droplets, there is a decrease in sebum excretion, the hypertrophy process is not required. The skin pores revert to a much smaller size and the skin becomes smooth and fine.

As acne lesions tend to subside spontaneously after puberty, some patients do not need a maintenance dose. But, if a patient is in his mid-teens, when the sexual characteristics have yet to fully develop, it may be necessary for replacement therapy to be implemented. This maintenance dose, can be lowered, or increased with the clinical symptoms. A maintenance dose will not only act as a preventive measure against sporadic eruption, but the extra pantothenic acid will help to ease the relative deficiency state, and likely improve the general health of the patient.