Current Comments

Acne Vulgaris-The Adolescent's Albatross

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King Tut had acne. His tomb contained remedies to fight the disease. In the fourth century AD, the court physician of Theodosius the First advised acne victims to wipe their "pimples" with a cloth while watching a falling star. The pimples would then "'fall from your body.'"²

The number of people who experience acne is astronomical. Estimates vary, but most experts agree that between 50 and 90 percent of all teenagers suffer mild to severe acne.³⁻⁵ Some believe that everyone gets some acne—if only one or two pimples—during the teen years.^{3,6} In the US in 1979, an estimated 15.5 million teenagers had acne.⁷

As if this wasn't enough, the scourge of acne remains with many people in their 40s, 50s, and even 60s. And for others the scars, both physical and emotional, are permanent.

Although some people may think of acne as a symptom, it is in fact properly classified as a disease. And it takes many forms. The most common one is known as acne vulgaris. (Vulgaris, a Latin word, means common, or ordinary.) Though not life-threatening, it can be emotionally damaging, and in some severe cases can lead to depression. It is difficult to estimate how much such a disease can affect one's life. If you have experienced acne, as I did, you will easily recall the anxiety it produces in anticipation of social events. Adolescents may find it especially traumatic on the night of a prom or their

first date. But the most frustrating aspect of acne is our continued ignorance of its real causes and, as a consequence, the failure of science to produce a total cure or to prevent its occurrence.

The basic physiological facts of acne seem to be well understood. Acne can be simply described as an "inflammatory disease of the sebaceous glands."8 But unfortunately, as with so many other diseases, no one has been able to determine why acne occurs. Nor is it known why there is such variation in the severity of the disease. Compared to the degree and duration of acne in one of my sons, my own case of acne was trivial. I mention this since some experts believe that acne may have a hereditary component. But this connection has not been clearly established. According to James E. Rasmussen. State University of New York. Buffalo, "A history of acne in both parents is often obtained in teenagers with severe acne but definitive genetic studies have not been performed."9

According to Gerd Plewig, University of Munich, Federal Republic of Germany, and Albert M. Kligman, University of Pennsylvania, acne is triggered by the increased hormonal activity that signals the onset of puberty. Males generally suffer the most severe cases. Acne occurs mainly on the "oily" parts of the body—the face, neck, and back. Usually, the more oily the skin, the worse the acne. Oily skin is easily identified by its greasy feeling and, often, the shine given off by the oil. In the majority of cases, acne clears up spontane-

ously in the late teens and early 20s.6 (p. 326) The average duration of acne is about six years—from puberty at about age 12 or 13 to late adolescence, or age 18.9

In order to understand the drama of acne, it is necessary to first understand the stage on which it is played. This "stage" is actually the pilosebaceous unit, which consists of a hair follicle and a sebaceous gland. All hair follicles, regardless of their location on the body, are accompanied by a sebaceous gland.

The hair follicles in which acne occurs, like any hair follicles, consist of a sort of tubular canal that encloses the hair that grows from the base. This follicle, like the surface skin, is lined with a layer of cells, or epidermis. As mentioned in a recent essay on baldness, this cell layer in a hair follicle continually undergoes a sloughing-off process. ¹⁰ In this process the old cells are discarded and replaced with new ones. The old cells travel up the follicular canal and are discarded on the skin surface.

Located alongside or at the base of the hair follicle is the sebaceous gland. It empties sebum into the canal. Sebum, like the discarded epidermal cells, flows up the canal and is also discarded on the skin surface.

A semifluid substance composed largely of triglycerides, wax esters, and squalene (a cholesterol precursor), sebum has no apparent function, beyond, perhaps, lubrication. For example, it is common wisdom that water runs off a duck's back. Why isn't the water absorbed by the feathers? Sebum. It provides an oily layer that repels the water. In all furbearing animals, sebum provides the lubricating properties they need to survive.

There is no such obvious use for sebum in man, however, and researchers have no explanation for why we continue to produce it. Like the appendix, sebum is believed to be an evolutionary relic that has no useful modern function.¹¹ But while a relatively small percentage of the population experiences

appendicitis, acne is a high price to pay for an evolutionary relic. Sebum is secreted in all hair follicles of the body, as well as directly onto the skin in many places. The sebaceous glands located in the face are unusually large, however, and secrete a disproportionate amount of sebum.

The follicles in which acne occurs differ from normal hair follicles in significant ways. As mentioned earlier, the sebaceous glands in these follicles are much larger than usual. Consequently, they secrete sebum at a higher rate. At the same time, the hair size is generally much smaller than the canal size. In fact, the hair is often so small it is not visible. In addition, the epidermis lining the follicle is weak and poorly defined. With the onset of puberty, sebum secretion is increased, triggered by an increase in hormone activity. In particular, the hormone testosterone appears to stimulate sebum production.6,7

For reasons no one knows, the normal sloughing off of cells in the hair follicle goes awry in the acne-prone person. Instead of moving out of the follicle, the cells begin to glue themselves together. At the same time, they begin to keratinize, or become hard and horn-like. This keratinized mass of cells forms a plug in the follicle canal, which, with the addition of the sebum that cannot pass through, eventually becomes the well-known "blackhead" and pimple.6 (p. 58-60)

In scientific jargon, the blackhead and its counterpart, the "whitehead," are called comedones. A single blackhead or whitehead is a comedo. (The Latin derivation of the word is responsible for the unusual plural form.) The blackhead is, quite simply, a follicle "plug" of cells that has gotten large enough to be seen. Researchers believe that the black color is due either to pigmentation or oxidized keratin. Blackheads are "open" comedones, so named because the plug dilates the pore opening and protrudes on the skin surface. A "closed" comedo, or whitehead, is one

in which the pore opening has not been dilated. Closed comedones are frequently not visible on the skin surface. The plug, as already noted, is composed of sebum, keratinized cells, and a host of bacteria. Chief among these bacteria is *Propionibacterium acnes* (*P. acnes*).

Like sebum and keratinized cells, *P. acnes* is always present in acne. And although it is a necessary component of acne, its role in the causation of acne is not clearly understood. Researchers speculate that *P. acnes* metabolizes the triglycerides in sebum into glycerol and free fatty acids, which are comedogenic, or acne-causing. The free fatty acids, they suspect, cause the impactions to form.⁹

The closed comedo is the precursor of the later stage of acne commonly called pimples. The open comedo, conversely, presents little problem other than the fact it is unsightly. Left alone, it will eventually be reabsorbed into the skin. Too often, for temporary cosmetic reasons, these are squeezed open. This may lead to scarring.

Many closed comedones, however, undergo more dramatic changes when the already thin epidermis ruptures. Sebum is extremely toxic to the surrounding tissues, which usually, as a result, become inflamed. The result is a pimple, or, more properly, a papule. Like open comedones, the papules are gradually reabsorbed by the skin, a process that may take two to three weeks.

The inflammation caused by the rupture is sometimes, however, so severe that it causes the papule to fill with pus. This sort of pimple—which has a characteristic white center—is known as a pustule. Pustules, too, will eventually disappear on their own. Both papules and pustules, when severe, may leave scars.

In the worst cases of acne vulgaris, comedones, papules, and pustules may cover the face, neck, back, and chest. The upper thighs can also be involved. In very severe cases, often called cystic acne or acne conglobata, cysts are

formed as well. According to Anne Lucky, dermatology department, Yale University, who is engaged in research on hormones and acne, 12 the acne cyst is a large inflammatory mass which may extend between several follicles. It often heals with deep scarring. 12 Comedones that rupture will frequently reform around the plug that is usually left, and thus start a cycle of repeated eruptions.

In addition to acne vulgaris, there are other types of acne. Acne mechanica, for example, is caused by pressure on the skin. Tight-fitting clothes, such as shirt collars or headbands as well as backpack straps or helmet straps, can cause it. Farrington Daniels, Cornell Medical Center, points out that acne mechanica of the chin is also an occupational hazard for violin players. 13 Acne mechanica is also caused by chairs or hard seats, wide belts, bras, etc. The common practice of resting one's chin on one's hands can also result in acne mechanica. Happily, this type of acne can frequently be treated simply by removing the offending cause.

Acne venenata, or contact acne, occurs from contact with acne-causing (usually greasy or oily) products. Hair dressings used by men are often responsible for this type of acne. In women, acne cosmetica is caused by the use of various cosmetics.

A variety of substances have been found to cause acne. Plewig and Kligman explain, however, that "it is not necessarily the presence of special ingredients that makes one cosmetic more comedogenic than another, but higher concentrations and sometimes a mixture of comedogenic substances." (p. 227) Acne cosmetica also occurs in some Third World and Mediterranean infants, when their mothers routinely coat various parts of the body with lotions and oils.

Another type of acne, acne detergicans, is caused by overuse of soap. Plewig and Kligman report on this, noting, "It should be emphasized that

few ordinary soaps are comedogenic. However, acne patients are peculiarly susceptible to acnegenic contactants of all kinds. Even weak comedogens applied many times daily for long periods of time can aggravate the disease."6 (p. 231) They point out further that since many acne sufferers are also compulsive washers, this type of acne can be a problem more often than one would suspect. Acne can be caused by a variety of drugs or chemicals, sunlight, X rays, etc. Many women report a worsening of acne prior to their menstrual periods and during pregnancy. Researchers suspect this may be due to the hormonal changes associated with menstruation and pregnancy, but have been unable to adequately explain the phenomenon. 1,6

For those who suffer from acne, the burning question is, of course, how to treat it. People of my generation will certainly remember admonishments not to eat chocolate, to keep your hands off your face, and to wash frequently. Dermatologists now generally believe that the first part of this advice is questionable, and the last part invalid. They continue to debate the issue of diet, and views both pro and con still abound. In a 1969 study on the effects of chocolate, for example, James Fulton together with Plewig and Kligman, had subjects eat special chocolate bars daily. These bars contained ten times the amount of chocolate found in a normal chocolate bar. A control group ate a placebo bar, which appeared identical, but actually contained no chocolate. After a month, they found no significant changes in either group. They concluded that chocolate plays no role in acne. 14

Five years later, Bruce and Leila Mackie, Prince Henry and Prince of Wales Hospital, Sydney, Australia, refuted this study. They said the earlier study "did not make adequate allowance for the dietary properties of chocolate." They hypothesized that fats with higher melting points may reduce sebum flow, and thus cause the plugs that become comedones. They argued fur-

ther that in light of such an idea, it is really the fats in the chocolate that are the problem. Since the bars used in the first study were nearly identical in fat content, they believed that the study's results were meaningless. ¹⁵ The idea that high fat content in the diet is a cause of acne has been argued by other researchers as well. ^{16,17} Primary support for this idea rests on the fact that people in countries where low fat diets are normal, such as Kenya and Zambia, traditionally seem to have less acne. Still other researchers conclude that no real evidence exists for either position. ⁴

While the food issue is controversial, drug treatment, at least, seems to be progressing. Doctors no longer recommend watching falling stars, and their track record on acne is improving. It might be even better, except that, like so many other people with dermatological disorders, acne victims are "ideal" patients. They don't call doctors in the middle of the night, and they are rarely cured overnight—not, perhaps, the greatest incentive for developing a cure.

Researchers have experimented with numerous drugs in acne treatments. Some they have tried are sulfur products,9 liquid nitrogen,18 benzoyl peroxide, 6,9,19,20 tetracycline, 6,20-23 cimetidine,24 zinc,25 zinc and vitamin A,25 topical vitamin A acid (retinoic acid), 6.9,20,26 carbon dioxide slush,²⁷ and salicylic acid.6,20 Many of the drugs tried have proved useless. Most dermatologists today use benzoyl peroxide, tetracycline, salicylic acid, and topical retinoic acid in their treatments. 12.28 Most feel that retinoic acid is the most effective of all treatments. It works by preventing the sloughed-off cells in the follicle from sticking together. Technically, however, it is an exfoliant, or a drying and peeling agent.

Exfoliants were, for a long time, recommended in acne treatment. It was believed that by drying and peeling the skin one could remove, or pull out, the follicle plugs. This has since been shown to be untrue since the plugs are too deep-seated to be removed easily. Their other properties, however, make some exfoliants, such as retinoic acid, useful nonetheless.

Retinoic acid, like many exfoliants, is quite powerful, and can cause irritation. The favored method of application is in the form of a gel, which is applied to acne-prone areas once or twice daily. Its value, according to Lucky, is in preventing the formation of comedones. For this reason it must be applied to all acne-prone areas, not just on visible lesions. 12 It irritates the skin, causing a slight "blush" and a burning sensation. Treatment must be individualized to the patient, as tolerance varies from person to person. Lucky also notes that results take about three months, and, in fact, in the first few weeks of treatment the patient often looks worse.12 Retinoic acid is only available by prescription in the US. Generally, its use must be continued indefinitely. There do not appear to be any serious side effects associated with its use. However, doctors advise patients to avoid exposing treated areas to the sun, as sunlight can increase the irritation, and some discontinue treatment during the summer months, 12 Some evidence suggests that when used in high concentrations, retinoic acid can also increase the occurrence of sunrelated skin cancer.1

A relative of retinoic acid, 13-cis retinoic acid, is also a current target of acne research. Taken orally, this drug reduces sebum levels in patients, with a corresponding reduction in acne. Work in this area is quite new, and it appears, in fact, to be the "hot" area of acne research. So far, oral retinoic acid is used strictly in research. In 1980, a research front called Pharmacology of Oral Retinoids in Acne Treatment was identified in our ISI/BIOMED™ system. The two core papers identified with this front were published by Gary L. Peck, senior investigator, dermatology branch, and colleagues, National Cancer Institute (NCI), Bethesda, Maryland.^{29,30} Figure 1 shows a selected list of 1980 papers retrieved through ISI/BIOMED which cited the core papers. Both Peck's and the later studies have demonstrated dramatic reduction in sebum excretion with treatments of oral 13-cis retinoic acid. In fact, according to Peck, cases of acne which had previously resisted treatment were completely cleared up under his treatments.³¹ At the same time, side effects appeared to be minor.

Tetracycline, taken orally, has been used in acne treatments for many years. An antibiotic, tetracycline reduces the acne bacteria, which, in turn, reduces acne. In the small dose used in acne treatments, tetracycline appears to be safe for long-term use, 22 and is particularly useful in reducing papules. Comedones, however, are not affected by it. Like retinoic acid, it is only available by prescription, 19,22 Other antibiotics, such as erythromycin and clindomycin, are also frequently used. 6,12,28

Methods of acne treatment used in the past include estrogen therapy. X rays, ultraviolet light, and extraction of comedones. They have met with different degrees of success. Estrogen therapy has sometimes worked well in women. However, its feminizing effects make it unsuitable for use in men. By reducing hormone activity, it causes a reduction in sebum production. Ultraviolet light has not been particularly useful, although the usual reduction of acne in summer, thought to be a result of exposure to sunlight, makes some clinicians reluctant to give up on these treatments altogether.

X-ray treatment warrants special comment because its abuse in the 1930s and 1940s appears to have caused many cancers. 32.33 Extraction, although it can reduce the size of acne lesions within minutes, is generally unsatisfactory, as it is nearly impossible to remove the entire plug. For the same reasons, the age-old home treatment of squeezing pimples is frowned upon. 6.9 According to Daniels, people who squeeze pimples usually do it frequently, which often results in severe irritation. 13

One of the folk "remedies" for acne, not mentioned in the scientific literature, is based on the myth that sexual in-

Figure 1: Fifteen of the 35 1980 papers assigned to the ISI/BIOMED™ research front #80-2577, Pharmacology of Oral Retinoids in Acne Treatment.

Cunlifie W J. Acne vulgaris: pathogenesis and treatment, Brit. Med. J. 280:1394-6, 1980.

Cunliffe W J, Kearney J N & Simpson N B. A modified photometric technique for measuring sebum excretion rate. J. Invest. Dermatol. 75:394-8, 1980.

Drugs for acne. Med. Letter Drugs Ther. 22:31-2, 1980.

Gibson J R. The treatment of acne. J. Antimicrob. Chemother. 6:568-70, 1980.

Gomez E C & Moskowitz R J. Effect of 13-cis-retinoic acid on the hamster flank organ.

J. Invest. Dermatol. 74:392-7, 1980.

Hollander A. What's new in American dermatology. Hautarzt 31:411-8, 1980.

Jones H, Blanc D & Cunliffe W J. 13-cis retinoic acid and acne. Lancet 2:1048-9, 1980.

MacKie R M & Dick D C. Synthetic retinoids for acne. Lancet 2:1300-1, 1980.

Melski I W & Arndt K A. Current concepts—topical therapy for acne.

N. Engl. J. Med. 302:503-6, 1980.

Orfanos C E. Oral retinoids—present status. Brit. J. Dermatol. 103:473-81, 1980.

Peck G L. Retinoids in dermatology—an interim report. Arch. Dermatol. 116:283-4, 1980.

Plewig G. Effects of the aromatic retinoid Ro-10-9359 and of 13-cis retinoic acid Ro-4-3780 on the size of sebaceous glands in the Syrian hamster. Arch. Dermatol. Res. 268:239-46, 1980.

Plewig G, Wagner A & Braun-Falco O. Oral treatment of severe forms of acne with 13-cis-retinoic acid. München. Med. Wochenschr. 122:1287-93, 1980.

Strauss J S, Stranieri A M, Farrell L N & Downing D T. The effect of marked inhibition of sebum production with 13 cis-retinoic acid on skin surface lipid composition.
J. Invest. Dermatol. 74:66-7, 1980.

Wagner A & Plewig G. 13-cis-retinoic acid: pharmacologic and toxicologic finding in treatment of severe forms of acne. München. Med. Wochenschr. 122:1294-300, 1980.

While I have explained in earlier essays how we identify research fronts in the ISI/BIOMED system 1.2 let me reiterate the key points here. By referring to the ISI/BIOMED lindex to Research Front Specialties (1981) available for \$15.00 from ISI \$\frac{8}{2}\$ under the word acne, I could quickly determine the existence of specialty #80-2577. By simply keying in this number on my portable terminal, I was immediately informed that in 1980 there were 35 papers (hits) assigned to this classification.

The basis for the automatic classification was the clustering of the two key or core papers on the subject by Peck et al. Without repeating the rationale for co-citation clustering, suffice it to say that these core papers were not only cited at least 12 times (citation threshold) in 1980, but they were also commonly co-cited. Once they were identified as core papers, they helped us retrieve the papers listed here.

If you wish to continue the search in 1981, you can of course do this by keying in the same research front number. You limit the search to 1981 by keying in "PY-81" as a search term. In this instance, you will find that in 1981 there have been 14 papers assigned to this research front already. A selective listing of these is shown in Figure 2.

It is of interest to note that many of the articles listed in Figure 1 were also assigned to research front #80-0445. Retinoids and Cancer. This illustrates one of the many ways this self-organizing cross-reference system operates. (Incidentally, there were 274 papers assigned to this classification in 1980.)

A key point to observe is that we are not using title words to index these papers. While most of the papers contain one or more variations on the terms "retinoids," "oral," or "acne," many do not. We could of course use ISI/BIOMED to find all papers containing these terms, but you would obtain a more, or less, focused list, depending upon your choice of terms. For example, the simple combination "acne" and the stem "retinoi-" produced only five papers in 1980.

Such a search certainly would not have retrieved the article "What's new in American dermatology," a review article with 42 references. Nor would you have found other directly relevant papers. If you had simply searched under the word "acne," you would have retrieved 89 papers, which is clearly too many if your purpose is to obtain a more focused list of papers.

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- ABCs of cluster mapping. Part II. Most active fields in the physical sciences in 1978. Current Contents (41):5-12, 13 October 1980.*

tercourse "cures" acne. Considering the increase in adolescent sex during the past few decades, there does not appear to be any evidence that there is a causal relationship involved. The myth is undoubtedly fostered by the fact that acne

generally disappears at about the same time that sexual activity begins.

For those suffering from severe cases of acne, consulting a dermatologist is recommended. Both Lucky and Kligman believe that nearly all acne can be

^{*}Reprinted in: Garfield E. Essays of an information scientist. Philadelphia: ISI Press, 1981. 4 vols.

Figure 2: Selected papers from the 1981 ISI/BIOMED™ research front #80-2577, Pharmacology of Oral Retinoids in Acne Treatment.

Fritsch P. Oral retinoids in dermatology. Int. J. Dermatol. 20:314-29, 1981.

Frolik C A, Swanson B N, Dart L L & Sport M B. Metabolism of 13-cis-retinoic acid.

Arch. Biochem. Biophys. 208:344-52, 1981.

Gomez E C. Differential effect of 13-cis-retinoic acid and an aromatic retinoid (Ro-10-9359) on the sebaceous glands of the hamster flank organ. J. Invest. Dermatol. 76:68-9, 1981.

Plewig G & Wagner A. Anti-inflammatory effects of 13-cis-retinoic acid. Arch. Dermatol. Res. 270:89-94, 1981.

Weissmann A, Wagner A & Plewig G. Reduction of bacterial skin flora during oral treatment of severe acne with 13-cis retinoic acid. Arch. Dermatol. Res. 270:179-83, 1981.

successfully treated today, and that no one need suffer from it anymore. 12,28 The specialist may employ one or more of the ameliorative treatments mentioned above, and should also dispassionately try to make the patient realize that the condition will disappear with time. If the patient has serious scarring, dermabrasion, in which the surface of the skin is frozen and then removed by a rapidly rotating diamond wheel, may be a possibility. 13,34 Various types of surgery are also available to remove or mask scars. One of the most current is the injection of collagen under acne scars to "fill in" the holes. 13

For those with less serious cases of acne, there are a variety of over-the-counter products available. Some are useful; many are not. A recent report issued by an FDA advisory panel on acne listed only three ingredients found in such products as useful. The three were sulfur, sulfur/resorcinol, and benzoyl peroxide. 35 Other researchers recommend salicylic acid as well. 6.9

Plewig and Kligman disagree with the FDA's recommendations of sulfur products. Although sulfur and sulfur combinations have been used in acne treatments for over 2,000 years, they believe that it may actually aggravate, rather than help, acne.⁶ (p. 278) Controversy over sulfur preparations (not to be confused with sulfa drugs) has been fairly limited, however, as the interest in retinoids and retinoic acid has pushed sulfur to the background in acne treatments.

Commercial products generally fall into a few major categories—drying agents, cleansers and scrubs, antibacterials, and medications. According to a report in Consumer Reports, most of these products are ineffective. Cleansers and scrubs, no matter how they work, can only remove surface dirt and oils; they are unable to get in "deep" enough to disturb the root of acne, the plug. 1 As already noted, too much washing can actually be harmful. Harsh scrubs, report Plewig and Kligman, may irritate the skin unduly and even worsen acne. Their studies have shown that washing or not washing has little effect on acne.6 (p. 271-2)

Drying agents are primarily useless for the same reason: they only dry surface skin, and leave the plugs untouched. Likewise, externally applied antibacterials can only attack surface bacteria, and are unable to go deep enough to do any good.

The only commercial acne products that appear to be useful are those containing the four ingredients listed above, and researchers favor those containing benzoyl peroxide. Benzoyl peroxide, like retinoic acid, works to prevent comedones. It is therefore important for users to put the medication on areas they believe will develop pimples, and not just on pimples they already have.

One of the best things that can be said for acne is that it spontaneously decreases, and ultimately disappears, for most people with the culmination of the teenage years—at about age 17 or 18. However, in some cases it lingers on into the 20s. Except in the most severe cases, when it can be painful, acne is not so much a physical problem as a social and emotional one.

Daniels points out that acne occurs at a particularly bad point in life—a period in which teens are trying to establish their own identities, while parents are trying to "hold on" to their children. Acne can often become a "weapon" for both sides, he adds. And, of course, acne occurs just when teens are acutely aware of attracting the opposite sex and personal appearance seems most important. That incontrovertible fact of life increases the importance of finding a cure or preventative. We can only hope that researchers will soon be able to tell us why acne happens, as well as how.

On a national level, NCI presently supports research on retinoid therapy for acne. According to Florence Karlsberg, science writer at NCI, Peck is conducting studies to evaluate the toxicity, effectiveness, and mechanism of action of oral 13-cis retinoic acid in cutaneous disorders of keratinization. One of the disorders under study is cystic acne, ³⁶ which has previously been resistant to treatment. Two papers reporting on this study form the ISI/BIOMED co-citation cluster mentioned previously.

Unfortunately, acne research is generally a neglected area. According to Daniels, part of the reason for that neglect is due to emphasis given by granting agencies to diseases that kill. 13 Acne does not, of course, kill. But I'm sure that many people would argue that it can certainly make life miserable and, where depression is involved, lead to death.

For readers who want more information, acne research is reported in the Journal of the American Academy of Dermatology, Archives of Dermatology, British Journal of Dermatology, Journal of Investigative Dermatology, and Dermatologica, as well as numerous other medical journals. These leading dermatology journals are covered in the Life Sciences and Clinical Practice editions of Current Contents® (CC®).

The lack of significant breakthroughs in acne research is reflected in the fact that there are few acne Citation Classics. Of course, the authoritative text by Plewig and Kligman, on which much of this essay is based, is clearly a classic in its own right. Since its publication in 1975, it has already been cited over 100 times. While these and other authors have been identified with some major discoveries in this field, we still have a long way to go.

The purpose of this essay has been to emphasize that point. And one can't tell where the breakthrough might occur. It may turn out, for example, that a search for a male contraceptive hormone might identify a compound that would not have the feminizing effects of estrogen therapy. It will be interesting to learn whether the field of immunopharmacology provides a solution to the ancient scourge of acne. As with so many other drug discoveries, an undesired side effect in testing for one disease may prove to be the desired effect for another.

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