TRADITIONAL TOPICAL TREATMENT OF ACNE

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Abstract. Few studies of topical treatment in acne stand up to modern scientific requirements, and several of those which do suggest that some modalities make acne worse rather than better. There is evidence that sulphur, soap, and light treatment prolong the course of illness. This also applies to some components of the vehicles used for acne medicaments. Fortunately, traditional treatment can be abandoned in favour of the superior benzoyl peroxide and retinoic acid.

A recent paper by Kligman & Mills (1) starts: — "Everybody knows that sunlight is good for acne" and goes on to show that it is not at all the case. During the last ten years grave doubts have been voiced regarding the efficacy of many other of our trusted modalities for the topical treatment of acne. Many of the medicaments used would fail to be accepted by our Ministries of Health if applications were submitted to have them introduced as new preparations.

The assessment of clinical experiments with acne agents is difficult, but real progress in the evaluation of topical medications for acne was started with the introduction of an animal model about ten years ago. It was found that application of a substance to the inner surface of the external ear of the rabbit results in the formation of comedones, and that this comedogenic effect parallelled the capacity for the formation of comedones on human skin. Furthermore, this animal test model could be used to evaluate the capacity of topical medications to loosen and cause the shedding of comedones (2).

TOPICAL MEDICAMENTS FOR ACNE

Topical applications should aim at reducing the number of comedones and the intensity of inflammation. Reduction of comedones was previously thought to be achieved through the peeling action of keratolytic agents, but soon after the introduction of retinoic acid it became apparent that peeling was not a prerequisite for the reduction of comedones caused by this preparation. Topical agents are discussed below according to the classification proposed by Kligman and Mills, which I feel has helped define the various therapeutic actions of topical agents.

Keratolytic agents attack fibrous keratin but have no comedolytic action (2, 3). Examples of such agents are sodium thioglycollate and sodium bromide.

Peeling agents cause peeling by virtue of their irritant effects. However, they have no comedolytic activity. They do speed up the resolution of pustules.

Sulphur is the most popular peeling agent, and in the past has been a standard component of most acne prescriptions. It was assumed to be a keratolytic agent, but the peeling in fact results from local irritation (4, 5). It was assumed to be an antiseptic agent and while it is, it does not influence the follicular population of *Propionibacterium acnes* (P. acnes). Surprisingly, it has been found to promote the formation of comedones in the rabbit ear and possibly in man (5). Why has sulphur been used so universally by dermatologists? It promotes the resolution of pustules and, thus, by gross assessment there is quite rapid improvement. On the other hand, the interval between the formation of a comedone and its transformation into a pustule is about four months. Neither the observer nor the patient will attribute the pustules to a treatment four months earlier.

Comedolytic agents loosen comedones already formed and thus reduce the formation of future pustules. Retinoic acid (p. 65) and salicylic acid are the best examples of comedolytic agents. Salicylic acid has been used for a long time but in concentrations which have been too low to exert any comedolytic effect. Comedolytic activity can be achieved with 10% salicylic acid in a vehicle of ethanol, or ethanol and propylene glycol. This preparation serves as an inexpensive alternative to retinoic acid (3).

Resorcinol used to be considered an effective agent for acne, but I have found no reliable study to support this contention. It is not comedolytic (3), and since it has been suggested that resorcinol could cause

myxoedema (6), there is at present no need for continuing to use it.

β-naphtol is not comedolytic, but interestingly when it is applied to one area of the skin sebum production may be reduced in other skin areas, suggesting that it has a systemic sebostatic effect (7). After treatment with β-naphtol comedones are more difficult to extract (8). Another drawback to the use of β-naphtol is the risk of systemic toxicity so that it should not be used on skin areas larger than 150 cm^2 (9).

Emulsion creams of the w/o type with a surplus of emulsifiers reduce the pressure required for extraction of comedones and can therefore be helpful in clearing comedo acne (10). Many components of creams and lotions are comedogenic and can cause "acne cosmetica" (11, 12). It is of obvious importance that these substances not be included in acne medications, but to date, I have only seen one company that has advertised that its retinoic acid has been compounded in a "non-comedogenic cream base".

Soap has often been recommended for acne, possibly because the blackheads look dirty, and most of the patients are seborrhoeic. But once again, the obvious advice may turn out to be wrong. Soap can irritate the skin and may be comedogenic, so soap should not be used excessively (13).

PHYSICAL AGENTS

The comedogenic effect of tar, cocoa butter and sulphur in rabbit ears is promoted by sunlight. A similar enhancement has been reproduced in man with coaltar and squalene (1). Sunlight alone has the same effect (14), but sunlight is a popular modality for acne. Like sulphur, sunlight shortens the lifetime of the individual pustules, however, at the same time the number of comedones increases, and these in turn are transformed into pustules 3—4 months later. Some patients state that their acne gets worse after sun exposure, but as mentioned by Cunliffe & Cotterill (15) the resulting hyperpigmentation hides the lesions and thus the patient's morale is improved.

Superficial X-ray therapy reduces the size of the sebaceous glands. The effect, however, is shortlasting. A course of 800 r (HWL 0.85 mm Al) in divided doses causes a reduction in the size of the sebaceous glands that lasts for six weeks, while 1200 r may be helpful for as long as one year (16). The duration of the beneficial effect is short in view of the dosage, penetrating quality of the radiation, and the recently noted risk of resulting thyreoid cancer (17).

While Grenz rays (HWL 0.025 mm Al) may help acne, even a dosage of 100 r given 16 times over a period of five weeks caused improvement in only half of those treated (18). Sagher & Tass (19) were slightly more optmistic after observing improvement in 71 of 100 cases of acne. Their treatment caused peeling, which possibly indicates an adjuvant effect of the Israeli sun.

In 1965 Strauss & Pochi (20) showed that intradermal injection of sebum and comedones caused marked inflammation, suggesting that bursting of the cysts is the trigger of deep inflammation in acne. Attempts at comedo extraction could make a small cyst explode. Provided inflamed lesions are avoided, comedo extraction, as shown by half-face treatment, is useful on the forehead and sometimes on the cheeks (21). Superfical acne improves, but deep acne becomes worse.

Mechanical acne is common and mechanical factors are nearly always involved in non-symmetrical cystic acne. Since mechanical trauma makes cystic acne worse, it is surprising that freezing with carbon dioxide pencils can promote the resolution of cysts (22). In spite of the effectiveness of this form of cryotherapy, at the present moment cysts are best treated with local steroid injections. Peeling with carbon dioxide slush was popular among dermatologists but certainly not among their patients and has for that reason been abandoned. Freezing has no comedolytic action.

CONCLUSION

A review of the agents used in traditional topical treatment suggests that the dermatologists to some extent have prescribed local applications, which made the patients happy by making their pustules disappear, but which made the patients come back because of their inherent comedogenic activity. Fortunately, the realization of this has coincided with the introduction of superior topical applications, which will be discussed by others in this symposium.

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DISCUSSION

Strauss, Iowa: As Chairman, I want to make a few comments. The first concerns the reported comedogenicity of sulphur in man. A study has recently been completed involving a much larger group of subjects than used by Kligman. One or two sulphur preparations was applied to the back of 40 subjects. A control base was applied on the other side. Histologic data derived from this study, which was done exactly as in Kligman's study, has shown that sulphur was not comedogenic under the conditions of the study.

Shuster, Newcastle-upon-Tyne: I would like to point out to Niels Hjorth that the rabbit ear assay has not in any way been validated. It merely shows that under certain circumstances blackheads develop in the rabbit ear.

Donsky, Toronto: I was just thinking of the days when they said that chocolate was no longer a factor in acne and I felt very badly because I could no longer say to my patients that food was causing their problems. And then sulphur came along and even though sulphur seemed to be helping my patients I was told that I could not use this any more. The next thing I knew, ultraviolet light was making my patients worse instead of better. The point is that as long as clinicians find that things are working we have to draw a very definite line between what is seen in rabbit ears and in human skin. There is no question that the laboratory can help us and that we should take some direction, but still we have to trust our own eyes.

Plewig, Munich: We need animal systems to study diseases, particularly acne, and at the present time there are very few animal systems available. One of the systems available today is the rabbit ear and in many aspects it confirms clinical observations. The one exception is that corticosteroids are potent comedoge-

nic compounds in the human but they are not in the rabbit. The rabbit ear is not only good to produce comedones, but it can be used to study the effects of comedolytic agents. The effects of vitamin-A-acid and benzoyl peroxide are very well shown in this animal model.

Leyden, Philadelphia: There are certain chemicals such as chlorinated naphtalenes and coal tar that are known to produce outbreaks of comedonal acne. These compounds cause comedones in the rabbit ear and in no other animal model that we know of. There are other chemicals such as vitamin-A-acid that are effective in unseeding comedones in acne patients. Vitamin-A-acid will work in the rabbit ear and in no other experimental animal model. There are many other chemicals which have been said to be effective in the past which do not work in the rabbit ear model. At least the results of the rabbit ear studies force us to examine concepts. It gives us a way of beginning. Many of you probably agree that many cosmetics may be harmful for acne. Cosmetic agents have been shown to produce comedones in the rabbit ear, confirming clinical impression. Therefore, the comedone that is formed in the rabbit ear is not the same as the human in one important respect; it is not as tightly impacted as it is in the human.

There are agents such as benzoyl peroxide which are somewhat effective in the rabbit ear and which appear to be only marginally effective against comedones in the acne patient. There also are some chemicals that probably will produce low-grade comedones in the rabbit ear and are unlikely to produce comedones in the human. The rabbit ear model does at least provide us with an experimental method for investigating one aspect of the disease. We can test a variety of chemicals and agents for potential comedogenicity and also for potential comedolytic activity. Of course the data has to be taken to the human subject and there the situation is much more difficult. Like all models the rabbit ear system is not the same as the natural disease, but models are merely designed to help get insights. I think, if you consider the matter in this respect, you have to say that the rabbit ear model has been an advance. It has given us a way to look at things and forced us to re-think about other things that in the past people have just swallowed without thought.

Cunliffe, Leeds: One question concerns β-naphtol. I realize from what several people have said, it is very easy to accept, perhaps incorrectly, the occasional paper that comes out stating that certain drugs should be stopped. But is there anybody in this audience who really does continue to use e.g. β-naphtol, because of its renal problems? Certainly, in the United Kingdom this is not used at all.

Zachariae, Aarhus: In answer to your question about β-naphtol, we still use it in our department in patients with severe acne. We give them one of those old terrible mixtures of green soap, precipitated sulphur, β-naphtol, and vaseline. They apply it initially for 15 minutes, and then increase the time up to three hours. Afterwards, we put them on vitamin-A-acid. I think the patients are very happy with this regime.

Schaefer, Berlin: Dr. Zachariae, do you follow the status of the patients' liver function, because absorption of β-napthol is high and it is a potent poison?

Zachariae, Aarhus: I am much concerned about the status of the liver and I have done a lot of liver biopsies, but not in these patients. We have followed transaminase levels in some patients and these have not increased.