CLINICAL EVALUATION OF ANTIDANDRUFF FORMULATIONS

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DANDRUFF is the common name given to the scalp conditions produced when the continuous but normally imperceptible sloughing of the outer epidermal layers of the skin becomes grossly visible. The scale consists of desquamated epidermal cells, accumulated secretions and acquired soil. When there is no obvious overactivity of the oil producing sebaceous glands, the condition is called Pityriasis capitis or Seborrhea sicca; with excess oil production it becomes Seborrhea oleosa and if it is accompanied by an erythematous or eczematized involvement of the outer skin itself it becomes seborrheic dermatitis. Figure 1 illustrates this sequence.

Antidandruff preparations are intended for treatment of Seborrhea sicca (a) and Seborrhea oleosa (b). However, if the condition has progressed either through local eczematization (c) or has spread to other body areas of predilection (d), more than topical therapy is often required to achieve control.

The mechanics of dandruff formation are best illustrated in a cross sectional view of the skin. Normally, the gradual sloughing of the dead and hardened outer epidermis exactly balances the constant production of new cells from the germinal layer below. Figure 2, which shows comparative photomicrographs of the skins of several animals and man, illustrates that this property of continuous growth is common to all animal skins, but it also shows human skin differs from that of the lower animals. In the human, there are more layers of viable and partially viable cells between the living, germinative basal layer of the epidermis and the tough, outer, fully keratinized layer, and therefore, any disturbance in the balance established between the constant production of new cells and the rate of sloughing of the old may produce visible masses of epidermal cellular debris that we call "dandruff." This is not identical to animal "dander" which consists primarily of keratin flakes. Most animal skins do not have the relatively thick, tough epithelium characteristic of man but depend for their strength upon a more fibrous, more heavily haired subepidermal

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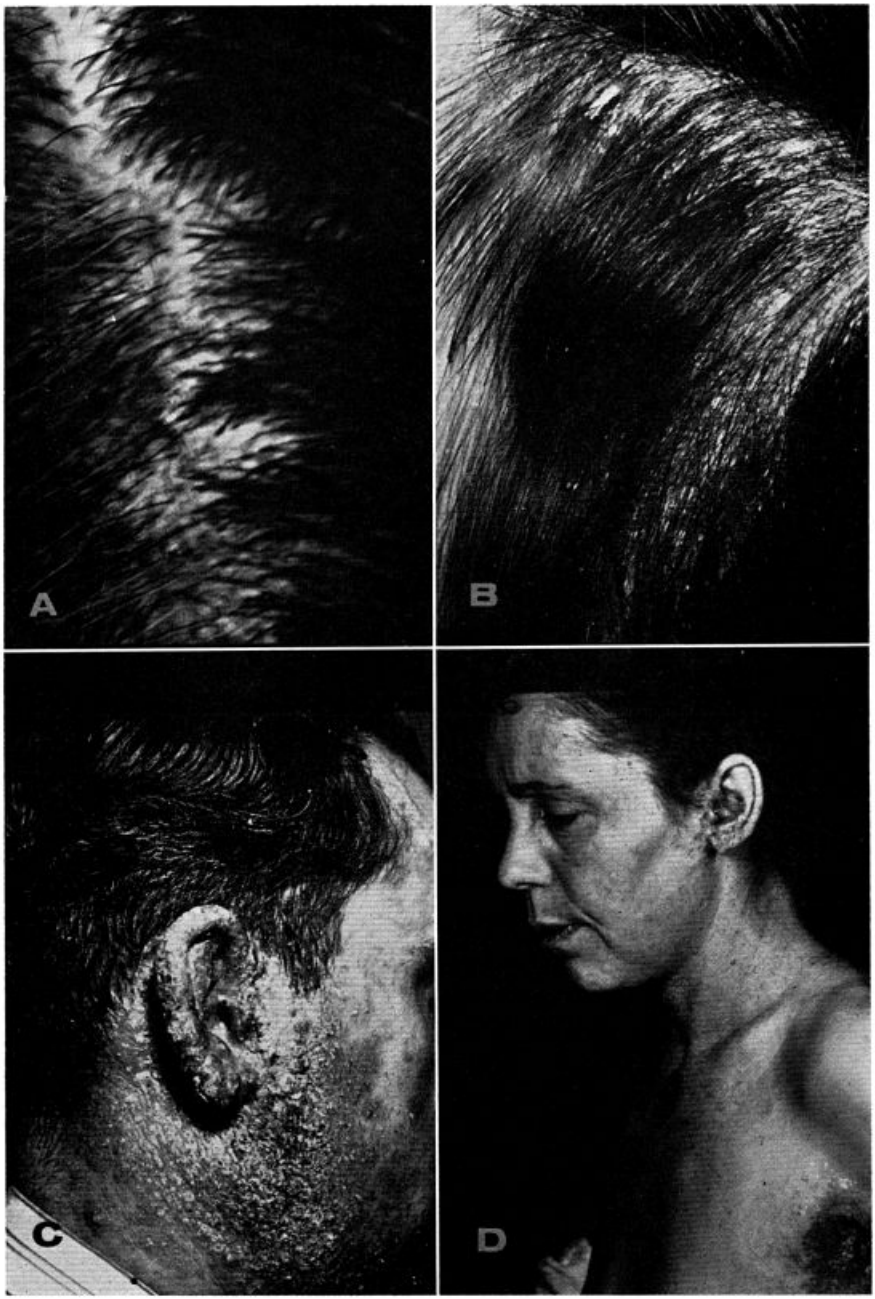

Figure 1.—Seborrheic diathesis. (A) Seborrhea sicca. (B) Seborrhea oleosa. (C) Seborrheic eczema—local. (D) Seborrheic eczema—other areas.

cutis. Another basic structural dissimilarity that may be responsible for a difference in epidermal desquamation is the relative lack of sweat glands in the animal skin, except in special areas. Animals like the cat and dog do not regulate their body temperature by evaporation of water from the entire body surface; hence there is no flow of water to wash continuously against and through the cellular structure, as is the case with the human epidermis. It is quite apparent from Fig. 2 that rabbit and guinea pig

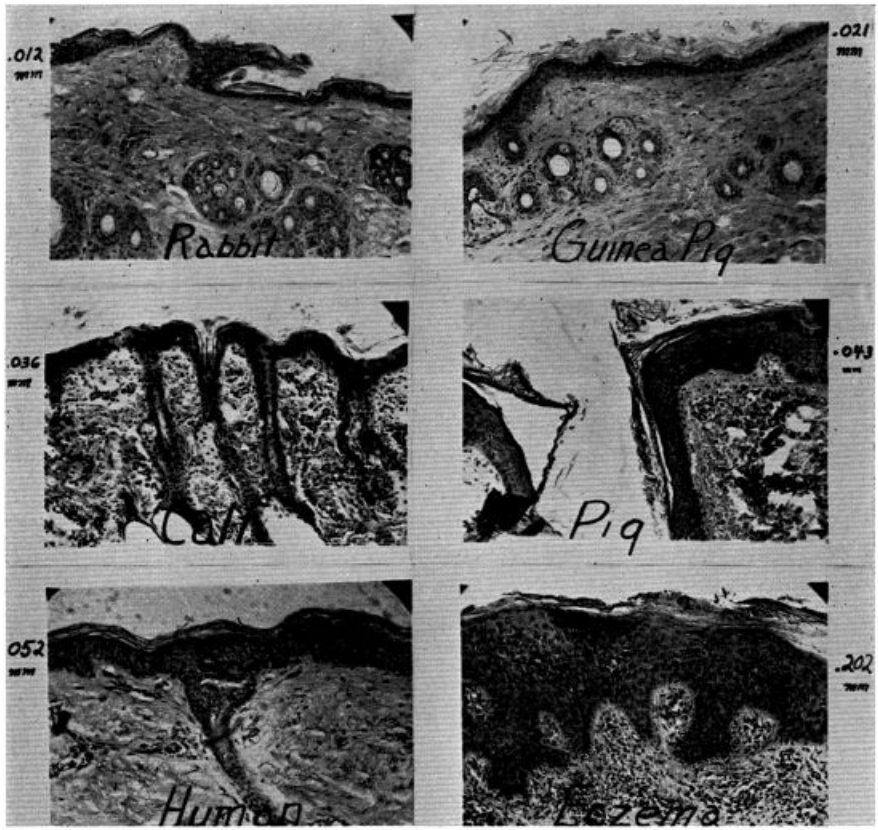

Figure 2.—Skins of Animals. (Credit: H. J. Spoor, *Proc. Sci. Sect. Toilet Goods Assoc. No. 36*, 20 (1961).)

skins are very different from human skin. The epiderms are so thin that it takes an extremely competent technician to obtain an adequate section. Calf skin approaches human more closely, but the hair structure is quite different. Pig skin, in thickness of epidermis is quite comparable to human, but the bristle structure is totally foreign. Normal human skin has a reasonably consistent epidermal thickness varying from 0.06 to 0.09 mm. except on the palms and soles (1), and is structurally quite similar in the infant and adult except for acquired maturity of dermal fibers. However,

the epidermis does respond quickly to irritation. The section labeled "eczema" shows a maximum thickness reached by one epidermis before frank eczematization and exfoliation occurred. Seborrheic eczema could appear this way.

Another important factor influencing dandruff formation is the amount and type of sebum secreted. This emollient, when properly dispersed, can smooth and flatten out dry horny skin layers without affecting normal desquamation. However, should sebum become excessive or accumulate at the pore openings the desquamating scale may adhere in visible oily masses. Dandruff is most apparent on the scalp or other hairy areas because sebaceous glands surround hair follicles and the sebum is discharged upon the hair shaft as a lubricant and protective coating. Sebaceous secretions also furnish lubrication to the non-hairy skin, but here the emollient is discharged directly upon the skin surface through pore openings that are associated with lanugo or primitive hairs. The oil is dispersed more broadly than in the hairy areas. The amount of sebum is influenced by the individual's genetic pattern, nutritional state and endocrine balance. Usually dark skinned individuals secrete more sebum than do those with lighter skins, the younger adult has more skin oil than the older and the male more than the female. Nutritionally, variation in the intake of fats or their impaired metabolism due to deficiency or improper utilization of certain vitamins may alter sebum flow. Specific foods, drugs or allergens may aggravate oil excess. Steroid hormones influence the development and function of the sebaceous glands. Generally, testosterone or the male type hormones promote both the growth and excessive function of the oil glands, while the estrogens or the female type hormones counteract both these actions. Work with the pituitary and the adrenal cortical hormones shows that these, too may have direct action upon sebaceous glands. The oil-rich, scale-laden scalp furnishes an excellent culture medium for many types of bacteria, some of which may bear causal relationship to the extension of simple dandruff to clinical seborrhea (2).

I have found it increasingly difficult dermatologically to separate simple scalp dandruff from the rest of the seborrheic diatheses, so to my mind, antidandruff agents must have therapeutic value. I think that:

1. The seborrheic state, in all its facets, stems from a common cause.
2. Some disturbances of the sebaceous secretion and epithelial keratinization are involved.
3. These disturbances may well be of allergic nature.
4. They are always found associated with bacterial and yeast invasion.

Furthermore, legally, if not medically, one of these yeast groups, Pityrosporum ovale, has been considered a causative agent of infectious dandruff. Accordingly, any product making antidandruff claims must be capable of destroying both these yeasts and certain associated bacteria (Staphylo-

cocci). Obviously, no product should be considered of medical value until it has proved itself to be clinically effective in seborrheic individuals.

In past years a useful yardstick for measuring the effectiveness of antidandruff agents has been their effect on yeast like organisms cultured from the scalp. The "bottle bacilli" are difficult to cultivate artificially unless the acid, oily, partially anaerobic conditions under which they grow naturally are simulated. Unfortunately, it has been our observation that even though the organism certainly occurs on the majority of normal male and many female scalps, it is not associated with seborrhea and dandruff in high enough frequency to establish causal relationship. The most apparent correlation we could find after studying 100 young men was that an increase in adherent scale was associated with an increased frequency of positive culture but that many of the subjects with no evidence of hair loss, dandruff or seborrhea showed positive cultures for the organism (3).

A broader bacteriological base than just Pityrosporum ovale cultures was needed. Therefore, we studied the scalp bacteriology of a group of patients with seborrhea to determine flora patterns. All individuals had routine scalp cultures made on three media: brain-heart, Sabouraud's maltose and Benham's wort agar. The dominant organisms were Staphylococcus aureus, Staphylococcus albus and Pityrosporum ovale yeasts. All individuals harbored the Staphylococci but there was an apparent male dominance of yeast infection susceptibility (2).

The next approach to the problem of evaluating antidandruff agents was to screen materials in the laboratory for their potency against the particular bacteria and yeasts isolated from seborrheic individuals. Typical results obtained on a laboratory screening are shown in Table I. Here measurements against the Staphylococci and several of the Pityrosporum groups are shown. The behavior of chlorinated phenols, quaternary ammonium compounds and anionic detergents indicates their failure to

TABLE I—LABORATORY COMPARISON OF GERMICIDAL AGENTS TESTED AGAINST ORGANISMS ASSOCIATED WITH SEBORRHEA

Agent	Concentration	Cup Plate Assay—Inhibition Zones, mm.				
				Pityrosporum ovale		
		Staph. aureus	Staph. albus	Type 1	Type 2	Type 4
Hexachlorophene (G-11)	0.35% lotion	24	30	Slight	0	0
Quaternary ammonium type	0.1% aqueous	30	32	23	Slight	Slight
Sodium alkyl sulfate (Duponol)	1.0% aqueous	22	17	Slight	Slight	Slight
Merthiolate	0.01% aqueous	23	20	25	...	...
Phenyl mercuric acetate	0.01% aqueous	23	26	39	...	...
Sodium sulfacetamide (Sebizon)	10% aqueous	Slight	20	28	Slight	Slight
Actamer type compound	1.0% glycol	38	42	52	33	26
Selenium sulfide (Selsun)	2.5% aqueous susp.	34	27	38	37	30
Polysulfide compound	3% alcohol	56	41	40	43	35

control adequately the Pityrosporum ovale. To obtain the broadest spectrum either a mercurial or some type of sulphur containing compound is desirable. This, of course, confirms clinical experience, because ammoniated mercury or sulphur preparations have been used widely for many years.

During the past two years we have found it worthwhile to culture the specimens taken from seborrheic scalps on an anaerobic bacteriological medium in addition to the other media. We have not yet screened antidandruff agents against the anaerobic Staphylococcus that dominates this medium.

In the past, we have relied heavily upon such laboratory comparisons. Laboratory study will separate the more effective antidandruff agent from the less, but it cannot guarantee clinical value. We have developed a panel type of comparative use test, wherein under controlled conditions subjects may compare clinically several products. This panel type of study has been sufficiently selective to differentiate between antidandruff agents that could not be separated by laboratory criteria. Normal male subjects are used because first, their short hair permits greater efficiency in scalp and hair sampling and secondly, the measurable factors found in dandruff conditions are more apparent in men. Details of this method have been published together with some general examples of the results (4), but further extensions of the work with some specific data on antidandruff formulations will now be given. Comparative data are collected and quantitated during clinical examinations of the subjects at definite periods after use of the products. During the test periods (weeks), the test products are randomized to minimize the effects of uncontrollable factors such as temperature, humidity and dust in the environment. A standard method of evaluation has been evolved through experience. The examination measures the more general hair and scalp features, such as alopecia, visible loose dandruff, adherent dandruff and scale, grooming and cleanliness, as well as specific hair factors, namely, color, texture, brittleness, oil content and others. Scalp skin conditions, e.g., tightness, seborrhea, irritation or induced sensitization, are recorded. Laboratory work on bacterial flora, hair fragility and oil content are also completed. Quantitation is obtained by grading all observations numerically in terms of 1 to 4. Real numbers assigned to grade clinical observations make subsequent data comparison possible.

Table II gives comparative data obtained for an individual subject. Shown are the examination values found after a control period during which no shampoo was used, after a similar two week trial period during which a germicidal shampoo was used, then again after a period during which a nongermicidal shampoo was used. It may be noted that use of the shampoo containing 1 % G-11 increased the apparent oiliness of the hair,

TABLE II—HAIR AND SCALP EXAMINATIONS (INDIVIDUAL EXAMPLE)

HAIR AND SCALP EXAMINATION

Name Individual Example Number E.O. - # 3

Age 40 Sex male Date 1959

	Water only (2 weeks)	Germicidal Shampoo	Non-germicidal Shampoo
General Appearance			
1. Alopecia (degree of baldness)	25%	20%	25%
2. Visible Loose Dandruff	2	2	2
3. Adherent Dandruff and Scales	3	2	3
4. Grooming	fair	fair	fair
5. Cleanliness	2	3	2
Special Hair Condition			
1. Color	brown	-	-
2. Texture	fine-straight	-	-
3. Estimate of brittleness	2	2	3
4. Oil Content	2	4	2
5. Hair Dressing Evidence	none	none	none
Specific Scalp Condition			
1. Tightness of Scalp - (# 4 - loose)	3	2	3
2. Scalp Skin Condition	fair	good	good
3. Evidence of Seborrhea	2	2	3
4. Evidence of Irritation	none	none	none
5. Evidence of Sensitization	none	none	none
6. Additional Comment (optional)			
Bacteriological Findings			
1. Pityrosporum ovale Count	70	7	3
2. Aerobic Bacteria Count	430	200	450
3. Brush Breakage - (# hairs)	7	13	15
4. Unsaturated Oils (% olive)	2.6	2.1	3.2

although this was not confirmed in this individual instance by an increase in the measured unsaturated oil. Both shampoos increased breakage over that found following the water controls. Both shampoos reduced the Pityrosporum ovale count, but only the G-11 containing shampoo reduced the total aerobic bacteria count.

To help equalize the effects of individual variation, the data from an entire subject panel may be averaged for comparison. In the next table (Table III) the averaged values from 11 subjects are compared. Shown are values after water controls taken one year apart, soap shampoos without

and with G-11, cream shampoo with G-11 and an Actamer containing shampoo. There is also a data series obtained after the same subjects had used alcoholic hair dressing antidandruff preparations, rather than the shampoos. The preparations were with and without antibacterial additives, and the antibacterial preparations were with and without added sulfur compounds. The preparation with no added antibacterial agent was used by the subjects for two two-week periods spaced one month apart.

TABLE III—COMPARISON OF ANTIDANDRUFF AGENTS BY QUANTITATED CLINICAL CRITERIA

	Average Values for Subject Panel—(Graded 1 to 4)									
			Shampoos				Alcoholic Hair Dressings—Antibacterial		Alcoholic Hair Dressings—Without Antibacterial Agent	
	Water Controls #1	Water Controls #2	Without G-11	G-11 Soap	G-11 Cream	Actamer	With Sulfur	Without Sulfur	#1	#2
Clinical Criterion										
Loose dandruff	2.1	2.1	1.3	1.4	1.1	1.5	2.1	2.2	1.4	1.4
Adherent scale	2.0	2.5	1.7	1.6	1.6	2.0	2.2	2.2	1.5	1.6
Hair brittleness	1.6	1.8	1.8	1.6	1.7	1.4	...	...	1.9	2.4
Hair oiliness	2.4	2.4	2.1	2.3	2.2	2.0	...	...	2.4	2.2
Scalp cleanliness	2.2	2.5	3.1	3.2	3.0	2.4	...	...	1.3	1.4
Scalp looseness	1.9	2.4	2.1	1.9	1.9	2.2	...	...	2.2	1.8
Scalp redness	1.9	2.1	1.5	1.4	1.1	1.5	1.9	1.6	1.0	1.1
Laboratory Criterion										
Pityrosporum, subjects, %	36	54	10	20	10	10	18	36	47	40
Aerobic bacteria count	545	496	134	121	+	+	+	+	++	++
Brush breakage, hair#	15	16	11	10	8.6	7.7	11	8.2	11	11
Unsat. oils, olive, %	3.2	2.1	2.7	4.5	3.3	2.3	2.1	2.9	4.4	3.9

The tabulated data indicates that all shampoos, with the possible exception of that containing Actamer, reduced loose and adherent dandruff. The antibacterial hair dressing material, on the other hand, did not reduce dandruff, while the more bland hair dressing did. The observed findings on brittleness were equivocal. Hair oiliness was reduced by the shampoos, not by the alcoholic hair dressings. Shampooing added cleanliness, again excepting the Actamer-containing product. The hair dressings left the scalp less clean. No meaningful changes could be determined in scalp looseness, while scalp redness was decreased, following use of the shampoos and the bland hair dressing material. The Pityrosporum ovale culture data was quite clear cut. Shampoos reduced the percentage of individuals harboring the yeast; hair dressing materials did not, except where added sulfur was present. Aerobic bacteria counts behaved as expected and were reduced after use of an antibacterial containing preparation. Hair breakage was least after use of the cream shampoo and the sulfur containing hair dressing material. Unsaturated oils rose appreciably after use of the G-11 soap shampoo and the bland hair dressing material.

Tabulated data of the type shown often cannot withstand the statistician's onslaught, but they are meaningful to the clinician when they reflect observed individual trends. If the majority of subjects respond in a particular manner, and an arithmetic average of all subjects confirms the majority trend, the change is probably real.

Despite the apparent requirement that an antidandruff formulation be an effective cleansing agent and have demonstrable antibacterial powers, it is often found in practice that such products are not the most satisfactory for treating seborrheic individuals. Preparations such as the bland hair dressing shown in the preceding table are often most satisfactory therapeutically. These questions arise; is all dandruff the same and what type of individual has a susceptibility to this seborrheic state? It is known that Seborrhea capitis may be just an early clinical sign of some other skin conditions or it may remain an entity in its own right. Not known is the percentage of individuals with seborrhea that go on to develop other skin conditions or with what frequency other diseases have an associated dandruff condition. Such knowledge might help explain why antidandruff formulations are not uniformly effective.

During the past few years, I have taken particular note of the patients with dermatoses possibly related to Seborrhea capitis who have come to my office for treatment and have now made an analysis of these records. In addition to the seborrheic diatheses shown in Fig. 1, one finds dandruff associated with baldness, acne vulgaris, psoriasis, and infantile ezcema (Fig. 3). I have excluded from my study the minor number of hair loss cases whose cause can be determined and for which therapy is often effective. For example, these cases are those of alopecia due to psychic or physical trauma (a. areata, a. totalis), systemic disease (Lupus erythematosis) and specific infection (Tinea capitis). However, by far the major number of alopecia cases are those of male and female pattern baldness, and, for treatment of these, little can be done. Most of us associate dandruff with acne vulgaris because it, too, is a disease of the pilo-sebaceous system. Psoriasis is probably a hereditary disturbance in fat metabolism, yet we have a condition known as seborrheic psoriasis, and psoriatic scalp lesions are of very frequent occurrence. Infantile eczema, on the other hand, is almost entirely of allergic origin, yet it very frequently first presents itself as "cradle cap."

An analysis of data taken from my office records of appropriate patients with these particular dermatoses seen during 1960 and 1961 is given in Table IV. There were 90 individuals with male or female pattern alopecia. Eighty-three % of these patients had dandruff, the men even more than the women. There were 94 individuals with acne, but despite the fact that this is a pilo-sebaceous disorder, only 42 % had dandruff. Similarly, of the 15 cases of psoriasis, only 46 % had dandruff.

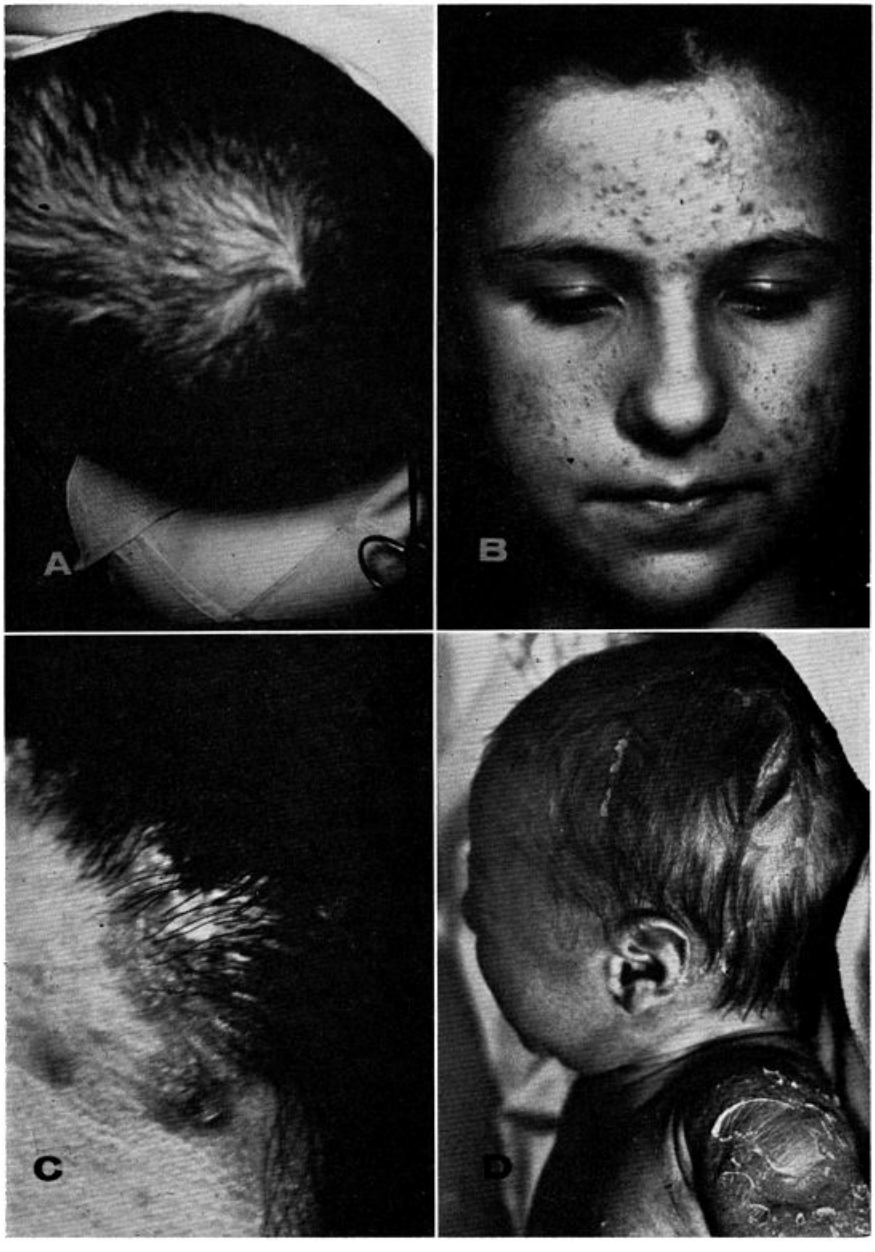

Figure 3.—Dermatoses related to seborrhea (dandruff). (A) alopecia. (B) acne. (C) psoriasis. (D) infantile eczema.

Eight infants with facial or body eczema attributable to a food allergy all had dandruff. Finally, there were 16 adults with severe seborrhea who

had no alopecia nor clinical sign of any other dermatologic disease. There were a total of 207 patients in the study group: 146 (70%) had dandruff, yet only 16 (11%) of these had only scalp seborrhea and no other skin condition.

I must conclude that dandruff is a very common sign that suggests an impending abnormal behavior of the skin or its appendages. The rationales for therapeutic use of antidandruff agents is therefore sound. A formulation should clean the hair, free the scalp of adherent debris and regulate the amount of residual scale and oil to retain healthful scalp conditions. Antibacterial properties either inherent in the formulation or as added germicidal agents are helpful. Mild keratoplastic or keratolytic action may help regulate epidermal sloughing.

TABLE IV—ASSOCIATION BETWEEN SEBORRHEA (DANDRUFF) AND RELATED DERMATOSES
(Private Practice—N. Y. City—1960 and 1961)

	Total	Male	Female
	Alopecia		
With seborrhea	75	46	29
Without seborrhea	15	6	9
	Acne		
With seborrhea	40	11	29
Without seborrhea	54	11	43
	Psoriasis		
With seborrhea	7	4	3
Without seborrhea	8	5	3
	Seborrhea Alone		
Adults without alopecia	16	7	9
Infants with food eczema	8	4	4

There have been a number of effective antibacterial agents developed, some of which compare favorably with the therapeutic standard, the selenium sulfide formulation. Further progress will come through use of antiallergens, similar in action to the topically applied corticosteroids. Not only analogs of hydrocortisone but also the sex hormones and their derivatives may prove useful. Topically applied vitamins and enzyme inhibitors may influence sebum flow. There is still room for antidandruff formulation improvement, but developmental study of each new ingredient must follow conventional design and be scrutinized on all facets of the dandruff disease process.

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