

THE EXPERIMENTAL PRODUCTION OF EXTERNAL OTITIS IN MAN*

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Another report from this laboratory (1) has outlined a practical clinical approach to the problem of external otitis. It has been found that a thorough and thoughtful diagnostic study of the individual case can, in many instances, remove that case from the ranks of "idiopathic" external otitis by supplying a specific etiologic diagnosis. However, at other times, it is impossible to make a specific diagnosis and, at our present level of knowledge, idiopathic external otitis continues to be a very real problem to both the otologist and the dermatologist (2).

The present experimental approach to the problem of external otitis was designed to determine the effects of maceration, primary irritancy, and allergic contactants. Under controlled experimental conditions, these various forms of mechanical and allergic trauma were perpetrated on the skin of the ear canals of healthy volunteers in an effort to produce clinical and histologic evidences of external otitis. The following outlines the technics and results obtained in this study of experimental otitis externa.

METHODS AND MATERIALS

The subjects used in these experiments were 79 normal adult male volunteers with no evidence of disease of the ears or ear canals.

Ear Plugs: Either a rubber or a plastic ear plug of the type used by swimmers was placed in one external auditory canal of each of 8 subjects. The plugs sealed the canals 24 hours a day, permitting no ventilation. Immediately after removal of the plugs, in from 1 to 4 weeks, biopsies were performed on the ear canals.

Tape: A rectangle of adhesive tape measuring approximately 4 by 8 millimeters was stuck on the wall of one external auditory canal (just proximal to the tragus) in each of 14 subjects. After periods of from 5 days to 6 weeks, it was removed and tissue for biopsy was taken from the area in each subject.

Tape and Ear Plug: Tape was applied to the wall of the ear canals of 24 subjects as described above. In addition, rubber plugs were placed in the canals to secure the tape and to seal the canals. After 2 to 4 weeks, the tape and plugs were removed and tissue for biopsies were taken from 16 of these men, including all who showed clinical changes.

Formalin: Formalin was swabbed over the skin of the external auditory canals of 12 subjects one time daily for 17 to 28 days. The first patients were exposed to 2% formalin, but this was later changed to 4%. Subsequent patients were swabbed with 4% formalin from the beginning. Tissue for biopsies were taken at the end of the experimental period.

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Halowax 1014: Halowax 1014, in a 50% concentration in mineral oil, was applied to the skin of the external auditory canals of 11 volunteers. The resultant irritation often necessitated periods of rest between series of applications. The material was applied 2 times daily for 3 to 9 days. Tissue for most biopsies were taken at the termination of treatment, but in 2 subjects this procedure was postponed until one month after the third (and last) application of Halowax.

3-n-Penta Decyl-Catechol: A single exposure to a 1:100 acetone dilution of 3-n-Penta Decyl-Catechol was used as an open patch test to produce a minimal allergic reaction in the skin of the external auditory canals of 10 subjects. The subjects were chosen because the presence and degree of their sensitivity were known. Tissue for biopsies were taken 72 hours after exposure to PDC.

In each instance, a record was made of the clinical condition of the skin of the ear canal before tissue for biopsy was taken. Each tissue specimen was *serially* sectioned and stained by routine hematoxylin and eosin.

RESULTS

Ear Plugs: Two of the 8 ear canals that had been sealed with ear plugs showed maceration of the skin. In one other canal which had been plugged for 4 weeks, a collection of cerumen nearly blocked the lumen. The amount of cerumen in the other canals was not notable. Three subjects demonstrated only a mild erythema and edema, one complained of pruritus, and two showed no clinical change and stated that they had noted no symptoms.

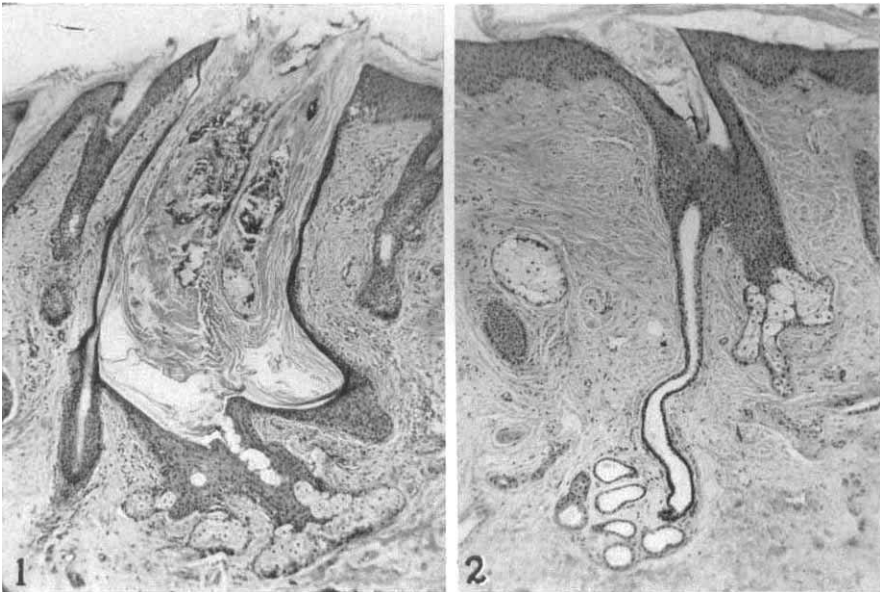


FIG. 1. Comedone formation in follicular orifice of ear canal. This subject had a continuous application of adhesive tape on the wall of the ear canal for 25 days. There was no gross evidence of clinical change. Magnification 51 \times .

FIG. 2. Dilated apocrine duct due to obstruction of follicular orifice following a 42-day application of adhesive tape. No evidence of clinical change. Magnification 56 \times .

The microscopic changes in the tissues removed from the volunteers who had worn ear plugs were not striking. A mild epidermitis was seen in some, a sparse infiltrate and a few plugged apocrine ducts completed the picture. In most, the changes were not more than one might expect to see in tissues removed from normal ear canals and they showed no correlation with the clinical findings.

Tape: There were no significant changes in the gross appearance of the skin of the external auditory canals when the adhesive tape was removed, even though it had been in place for 6 weeks in some instances. However, the histopathologic changes included periappendageal and perivascular lymphocytic infiltration, as well as "comedone" formation in many of the follicles (Fig. 1). These histologic comedones consisted of keratinous material in the follicle. Dilatation of the apocrine and sebaceous ducts was occasionally seen (Fig. 2). There was no evidence of epidermal vesiculation.

Tape and Ear Plugs: While half of the 16 tissue specimens studied showed no clinical change, the other half demonstrated the soggy maceration of the skin of the external auditory canal that has come to be recognized as the tropical form of otitis, the so-called "hot weather ear". Histologically this experimental otitis externa showed a rather consistent picture of hyperkeratosis, follicular plugging and acanthosis (Fig. 3, 4). Occasionally evidence of sebum retention was found (Fig. 5). Some specimens presented inflammatory changes in the corium. The

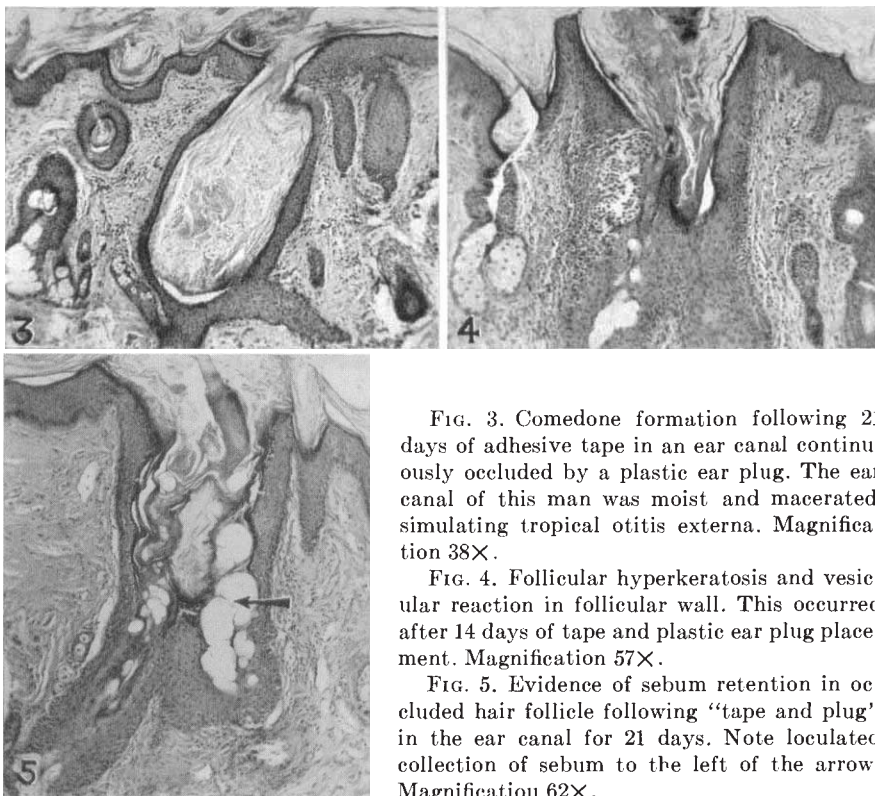


FIG. 3. Comedone formation following 21 days of adhesive tape in an ear canal continuously occluded by a plastic ear plug. The ear canal of this man was moist and macerated, simulating tropical otitis externa. Magnification 38X.

FIG. 4. Follicular hyperkeratosis and vesicular reaction in follicular wall. This occurred after 14 days of tape and plastic ear plug placement. Magnification 57X.

FIG. 5. Evidence of sebum retention in occluded hair follicle following "tape and plug" in the ear canal for 21 days. Note loculated collection of sebum to the left of the arrow. Magnification 62X.

microscopic findings were evident in 14 of the 16 specimens, so that changes were occurring even in the absence of clinical evidence of otitis. It is to be noted that apocrine miliaria was not seen.

Formalin: There were no symptoms and no evidences of clinical change in the men whose ear canals were being painted with 2% formalin. However, 4% formalin caused scaling and dryness in 5 subjects, eczematization of the skin of the canal wall in 2, and a sensation of numbness in 2, and of aching in 2. Two of the 12 had no clinical evidences of change, either subjectively or objectively. The striking histologic finding was the presence of follicular keratinous plugging (comedones) in all of the tissue specimens (Fig. 6). Furthermore, in half of them, random spongiosis and vesiculation of the follicular wall was commonly seen (Fig. 7). Mild dermal inflammatory changes accompanied this follicular wall reaction. The sebaceous and apocrine glandular tissue appeared to be unaffected by the formalin. However, the apocrine ducts were occluded in some instances as evidenced by ductal dilatation and casts (Fig. 8).

Halowax 1014: Every man receiving more than 3 applications of Halowax suffered eczematization and crusting of the skin of the ear canal. In 5 instances

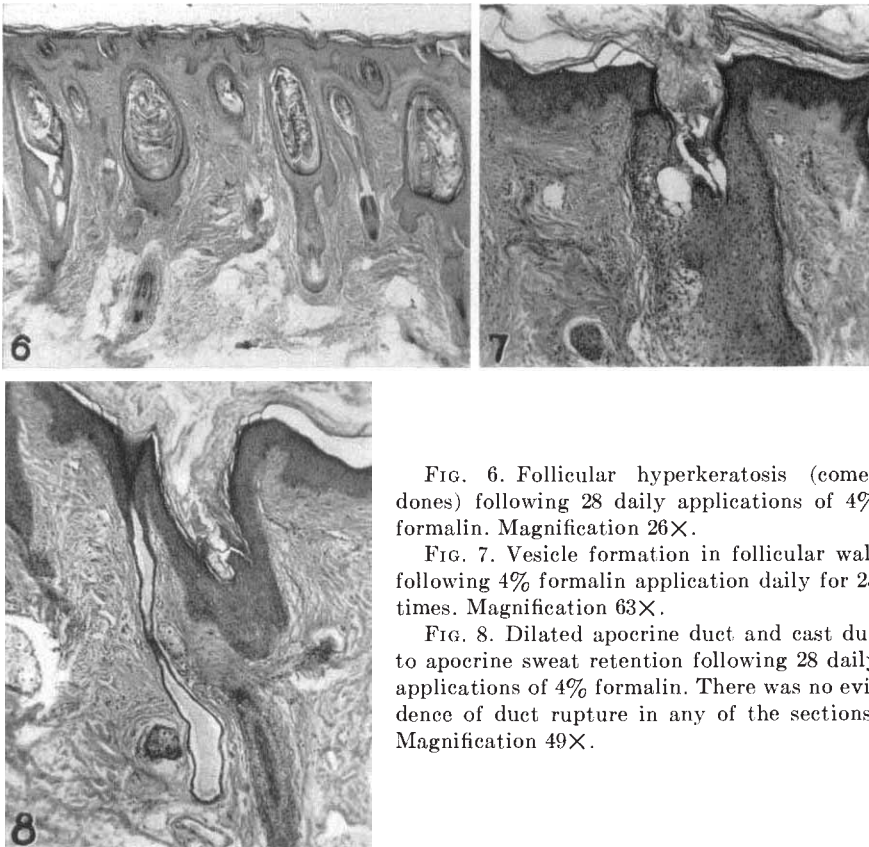


FIG. 6. Follicular hyperkeratosis (comedones) following 28 daily applications of 4% formalin. Magnification 26X.

FIG. 7. Vesicle formation in follicular wall following 4% formalin application daily for 28 times. Magnification 63X.

FIG. 8. Dilated apocrine duct and cast due to apocrine sweat retention following 28 daily applications of 4% formalin. There was no evidence of duct rupture in any of the sections. Magnification 49X.

this became quite acute requiring wet dressings and other symptomatic local therapy. Subjective symptoms such as pain and itching were noted by 7 subjects in this group. All instances of otitis produced by Halowax recovered after local therapy, although discomfort and objective signs of the dermatitis persisted for several weeks in 2 men.

Under the microscope, tissue specimens from the subjects who had received Halowax showed a remarkably constant picture. There was hyperplasia of the epidermis with hyperkeratinization and the formation of large comedones (Fig. 9). In a number of cases, there were vesicles in the epidermis. There was a marked inflammatory infiltrate of lymphocytes in the cutis, as well as a patchy basophilia and deposition of a mucinous-like material. While the ceruminous gland appeared unaffected, the sebaceous glands were absent or decreased in number in all specimens.

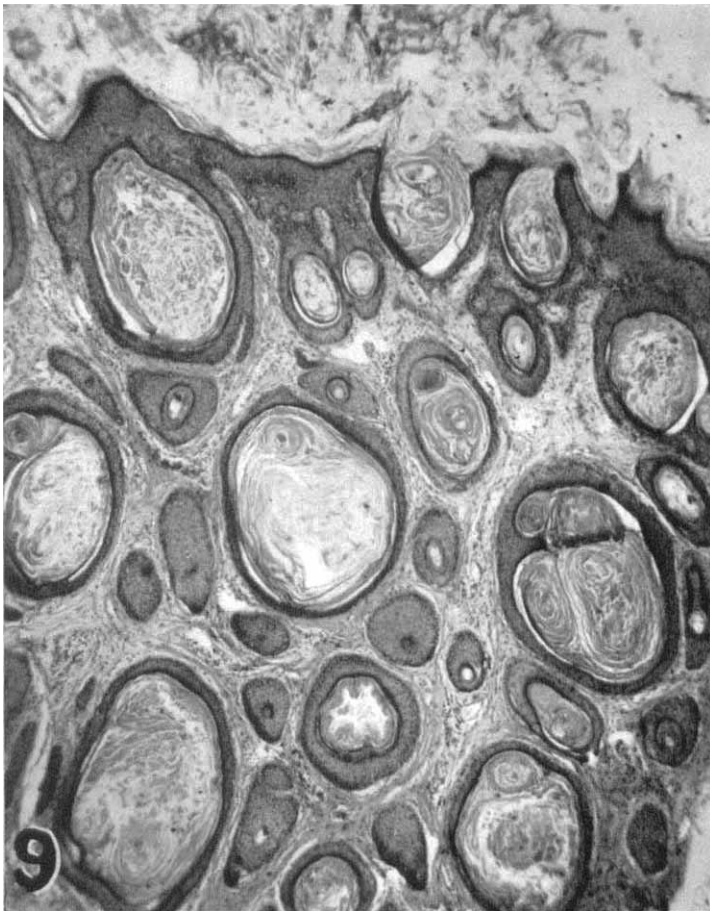


FIG. 9. Multiple comedone formation following application of 50% halowax 1014 two times a day for 3 days. Biopsy taken on 30th day in a dry crusted area. Magnification 50X.

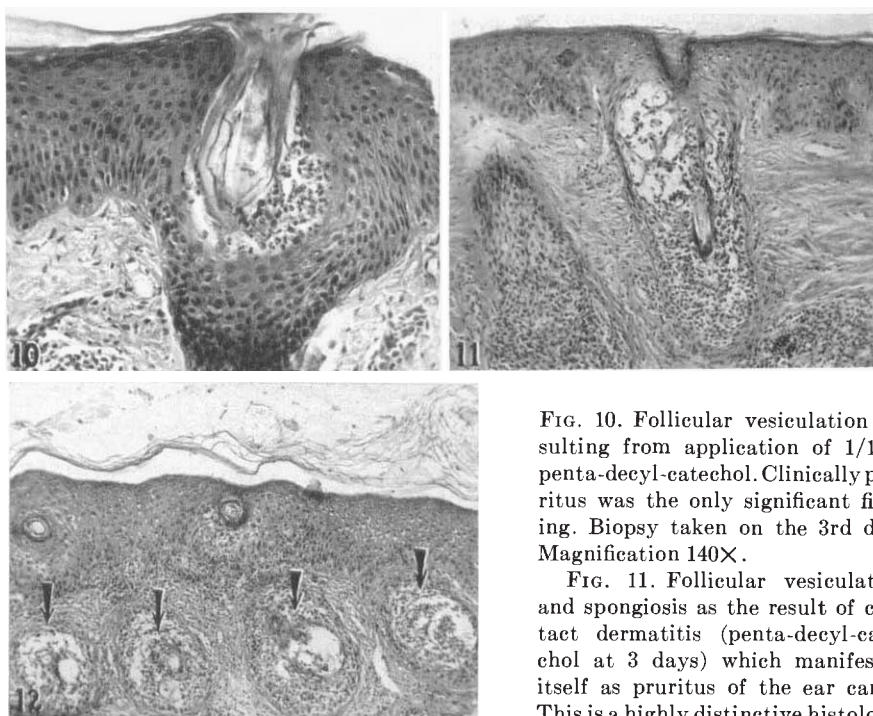


FIG. 10. Follicular vesiculation resulting from application of 1/1000 penta-decyl-catechol. Clinically pruritus was the only significant finding. Biopsy taken on the 3rd day. Magnification 140X.

FIG. 11. Follicular vesiculation and spongiosis as the result of contact dermatitis (penta-decyl-catechol at 3 days) which manifested itself as pruritus of the ear canal. This is a highly distinctive histologic

finding since vesiculation and spongiosis were *not* seen elsewhere in the epidermis following these "open patch tests". Magnification 90X.

FIG. 12. Contact dermatitis reaction *selectively* occurring deep in four hair follicles. The superficial epidermis is essentially unaffected. This biopsy was taken 3 days after the application of 1/1000 penta-decyl-catechol. Arrows indicate spongiotic follicular remnants. Magnification 64X.

3-n-Penta Decyl-Catechol: These subjects presented only pruritus and a slight erythema at the time of removal of tissue for biopsy, although in a few cases some edema was present.

On microscopic examination the changes were completely limited to spongiosis and vesiculation of the wall of the hair follicle (Fig. 10, 11, 12). The epidermis elsewhere was unaffected. There were no changes in the dermis or in the appendages, other than a moderate perifollicular inflammatory infiltrate.

DISCUSSION

It has been possible consistently to produce experimental otitis externa in man of the following types:

- (1) Maceration dermatitis—tape with ear plug.
- (2) Primary irritancy dermatitis—Formalin; Halowax 1014.
- (3) Allergic dermatitis—Penta-decyl-catechol.

Analysis of these three forms gives insight into the pathogenesis of some of the many variants of otitis externa seen clinically.

Maceration dermatitis is a common example of otitis externa seen in the tropical climates (3). Here, heat and humidity are the causative factors, and these were experimentally produced by the insertion of an ear plug and the concomitant application of adhesive tape to the canal wall. Remarkable, yet rapidly reversible, soggy "tropical ears" developed over a period of weeks. Yet individual differences in susceptibility are pointed up by the fact that this striking finding occurred in but 10 out of the 32 subjects whose canals were sealed. This is consonant with the observations of clinicians in the tropics who find many individuals immune to this affliction. Further clinical parallelism is shown by the fact that removal of the ear plugs was followed by prompt healing, identical to that seen in patients upon transfer from hot to cool climates. The moisture of apocrine sweat contributes to the problem in the sealed ear, since under these circumstances the humidity remains close to 100%. There is little doubt that high humidity in the canal is a critically important factor in producing certain forms of otitis externa. Actually the canal anatomy may be a contributing factor in some individuals in whom the canal is tortuous and of a small lumen. Negroes, conversely, have shorter, wider canals and are uncommon victims of a maceration dermatitis (4).

When this work was undertaken, it was realized that maceration of the ear canal never resulted in the miliarial syndromes, such as prickly heat, since the canal is entirely devoid of eccrine sweat glands. However, it was felt by us that apocrine sweat retention changes might evolve which would be important in initiating, maintaining or extending cases of otitis externa. We found nothing to support this view. It is true that apocrine duct plugging has been repeatedly produced, but this is asymptomatic and has not been associated with any histologic evidence of sweat duct rupture or retention vesicle formation.

Maceration greatly promotes the growth of bacteria and at times of fungi. Nevertheless, no true pyodermas or fungous infections were seen. The ear canal would appear to be reasonably resistant to the effects of over-growth of bacteria and fungi.

The second major type of reaction produced was the otitis externa resulting from the application of irritants. Both formalin and halowax produced eczematous reactions, at times moderately severe. These pictures histologically were generally non-specific, but in half of the formalin biopsies, spongiosis and vesiculation were seen in the follicular walls. The halowax specimens showed remarkable comedone formation, since this compound is actually acneigenic. These locally applied irritants demonstrated the production of a totally different reaction pattern in the ear canal skin. This pattern occurs but infrequently, yet it is a distinct reaction of the canal.

Finally, the most interesting findings come from the experimental production of a low grade contact dermatitis on an allergic basis. Here the reactions were clinically inapparent, save for the pruritus. At times erythema was evident. Hence, with this approach, it was possible to duplicate a most common problem, that is, idiopathic pruritus of the ear canal. Histologic studies revealed a uniform change: spongiosis and micro-vesiculation of the follicular walls. The surface

epidermis was entirely normal. This is the distinctive microscopic picture of early minimal contact dermatitis in the ear, and its presence in a biopsy from any patient's ear canal should urge further study of the patient's sensitivity to chemicals or materials coming in contact with the canal, e.g., matches, the varnish of "bobby pins", nail polish, and topical medicaments. Thus, a biopsy of the pruritic ear canal can be the significant clue leading to a diagnosis of dermatitis venenata.

CONCLUSION

Clinical and histologic observations have been made on a variety of forms of otitis externa experimentally produced in man. It has been found that maceration leads to a reversible "hot weather ear" in susceptible subjects. Furthermore, it has been shown experimentally that contact dermatitis of the ear canal may manifest itself solely as pruritus. In these instances there is a distinctive histologic picture of vesiculation of the wall of the hair follicle. This finding points up the diagnostic value of the ear canal biopsy.

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DISCUSSION

DR. ZACHARY FELSHER (Chicago, Ill.): I would like to ask what the effect was on the pathologic picture with application of the irritant formalin. Was there any difference in the pathology especially between the primary irritant, such as formalin, and the allergic dermatitis venenata reaction the presenter observed.

DR. BEN H. SENTURIA, (St. Louis, Mo.): I wish that I had had the courage to do what Drs. Shelley and Perry have done. Many years ago we thought of introducing exogenous bacteria into normal ear canals and of taking biopsies from normal and pathological ear canals, but we were not able to arrange it. I think the authors should be congratulated for their success in accomplishing this.

I am concerned about the interpretation of what was produced by the use of adhesive tape and plugging the ear canal for two weeks. I think one should be a little hesitant about calling it "hot weather ear." There may be a high humidity effect on the stratum corneum or there may occur thickening of the epidermis secondary to the adhesive, but I do not think these factors alone will cause otomycosis of diffuse external otitis. I would rather have heard them say that they had produced a dermatitis of the skin of the ear canal until they had demonstrated bacteriologically and pathologically, a disease which is similar to acute diffuse external otitis, or "tropical ear" or "hot weather ear."

The allergic reactions which were shown are very beautiful. We will go back over some of our specimens and see if we do not have similar material which may sub-

stantiate what has been said. It is conceivable that some of our material may be allergic with *Pseudomonas* infection superimposed.

I certainly enjoyed hearing this presentation.

DR. ELDON T. PERRY, (in closing): In answer to Dr. Felsher, I would like to say that the difference between the histologic pictures of primary irritation and of contact dermatitis was primarily one of degree. In contact dermatitis the changes were mainly in the epidermis with only minimal findings in the dermis.

I am hesitant to disagree with Dr. Senturia on the subject of "hot weather ear" because his experience has been so vast. However, we stated only that we produced the *clinical picture* of "hot weather ear," as it has been described in the literature. Moreover, in categorizing this "entity", I doubt that we can say, at the present, that there is any constant bacteriologic or pathologic picture. It is primarily a morphologic term for soggy, macerated ear canals.