

Human Sebum as Vehicle for Methylcholanthrene*

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Simpson, Carruthers, and Cramer (5) in 1945, demonstrated that methylcholanthrene when dissolved in anhydrous lanolin almost completely loses the power of inducing skin tumors in mice. It appeared desirable to Simpson, Carruthers, and Cramer to determine the reaction of the skin to the carcinogen dissolved in a medium that resembles sebum because, in their opinion, the sebaceous glands play an important role in experimental skin carcinogenesis. They chose lanolin because it represents the secretion of sebaceous glands of sheep; they assumed that the sebum of mice is similar to that of other species.

In connection with previous work (4) it appeared worthwhile to examine human sebum in the same way. To collect sufficient amounts of sebum from the skin surface of men is a difficult task. Large amounts of sebum, however, accumulate in the dermoid cysts of the ovary. These cysts are in part lined with skin epithelium, and large sebaceous glands secrete into the cavity of the cysts.

MATERIAL, METHODS AND RESULTS

The contents of dermoid cysts¹ were warmed slightly above body temperature; the oily yellow fluid could then easily be separated from the hairs and from the firmer whitish masses of desquamated squamous epithelium. Our assumption that this fluid represented chiefly the secretion of the large sebaceous glands was verified by determination of the lipid content in four specimens (100, 96.8, 99.5, and 99.6 per cent). This material was kept covered in the refrigerator; it was warmed before application until it was semifluid.

C 57 black mice (from Rockland Farms) were used. A 0.3 per cent solution of methylcho-

lanthrene was applied to an unshaved area 1.5×1 cm., on the back, three times a week, for 14 weeks, using the same technique throughout.

The mice were divided into four groups, using benzene, lard filtrate, sebum from dermoid cysts, and lanolin, respectively, as vehicles. The mice in the lard filtrate group were 88 days old, at the beginning of the experiment, all the others were 37 days old. The results are summarized in Table 1. In the benzene group all of the 35 mice developed cancer as was to be expected. Fifty per cent of them had cancer after 16 weeks; they all were dead after 35 weeks. The results in the lard filtrate group were similar to those reported in the literature. Tumors appeared considerably later than in the benzene group, but after 29 weeks, 50 per cent of the animals had tumors, and after 1 year all of them. In the group of mice treated with methylcholanthrene in sebum from human dermoid cysts, the results were very similar to those in the lard filtrate group. In the lanolin group, however, none of the 20 surviving mice developed a tumor.

DISCUSSION

There is a significant difference in the carcinogenic response to methylcholanthrene when dissolved in sebum or lard filtrate on the one hand, and when dissolved in lanolin on the other. Since all 3 solvents are non-volatile and of similar consistency, this difference in carcinogenic response deserves consideration. It cannot, in our opinion, be explained as a mere dilution effect. As far as sebum is concerned it may be in line with the differences between different batches of lard or, for instance, the difference in carcinogenic response to solvents like sesame oil and tricapyrylin. The use of lard filtrate and of dermoid sebum as vehicles led to delay of carcinogenic response when compared with benzene, while lanolin inhibited tumor formation in all surviving mice for a period of more than a year. The secretion of the sebaceous glands, which forms a film on the skin surface and on hairs, plays an important role in epidermal carcinogenesis. In the opinion of Suntzeff, Carruthers, and Cowdry (8) the sebaceous glands do not

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¹ The cyst contents were removed by hand from the ovarian dermoids. There was no extraction and no benzene was used.

merely represent portals of entry for the carcinogen but exert an influence upon the morphological and chemical condition of the epidermis. It is unknown how many factors may be involved in this influence and how far they would reinforce or counteract each other.

In human ovarian dermoids, which are tightly filled with sebum, carcinoma does occur. A survey of 1268 cases reported in the literature gave a percentage of 1.7 (3). In our own 328 cases, 4 carcinomas occurred. These tumors are squamous cell carcinomas, not of the ovary, but of the skin of the dermoid; they have all the ear-marks of skin cancer. It is unknown, whether or not the accumulated sebum contains a substance that induces these tumors, and it remains to be seen how far the same sebum, under the conditions of the mouse experiment, might be carcinogenic. Circumstances

when we consider, for instance, the frequency of anal carcinoma in dogs. The dog has large, peculiarly differentiated anal glands whose secretion accumulates in pouches.

There was no significant difference in the delay of carcinogenesis between the sebum series and the lard filtrate series. Lanolin, however, inhibited tumor formation in all surviving mice as it did in the experiments of Simpson, Carruthers, and Cramer (5). We do not know why in the experiments of Berenblum and Schoental (1) lanolin was much less inhibitory. Differences in the animals used, and differences in the brands of lanolin may be considered. The mechanisms of retardation and inhibition of carcinogenic response by non-volatile solvents in general, and by lanolin especially, await elucidation. The retarding effect of liquid paraffin suggests a dilution effect (1) but the great

TABLE 1

SUMMARY OF RESULTS

SOLVENT	NO. OF MICE	EFFECTIVE TOTAL MICE	NO. OF TUMORS	TIME OF FIRST TUMOR (WEEKS)	NO. OF TUMORS (IN WEEKS)					
					14	20	24	29	40	57
Benzene	35	35	35	7	13	27	33	35	35	35 (all)
Lard	30	26*	26	24	0	0	5	13	24	26 (all)
Sebum	35	28†	28	17	0	2	3	8	17	28 (all)
Lanolin	32	20‡	0		0	0	0	0	0	

* 3 died of infection, 1 of an accident.

† 5 died of infection, 1 was bitten to death, 1 died of unknown cause.

‡ 12 died of infection.

beyond our control prevent us at present from testing for carcinogenic, anticarcinogenic, or cocarcinogenic factors in human sebum. Numbers of other connected experiments that ought to be undertaken must, for the same reason, await a more propitious time. The study of sebum in relation to carcinogenesis, in our opinion, is of more than theoretical interest. The interaction between factors in the sebum and external potential carcinogens, when properly understood, might help in elucidating the genesis of some skin cancers, notably industrial cancers.²

The marked difference in carcinogenic response between human sebum (dermoid contents) and sheep sebum (lanolin) indicates possible species differences in the secretion of sebaceous glands. Simpson and Cramer (6) assumed that the sebum of mouse skin is similar to that of other species. Species differences as well as local differences in skin glands and their products suggest themselves

² Almost all skin cysts which are commonly called dermoids or atheromas, in reality are epidermoid cysts. No glands, sebaceous or others, are found in their wall, they do not contain sebum but desquamated skin scales only. They, therefore, do not belong to the topic of this paper.

differences between batches of lard and the difference between human sebum and lanolin, cannot be explained on such a basis. Weil-Malherbe and Dickens (9) have mentioned the possibility that the anticarcinogenic effects of animal fats might be caused by their content of phospholipids. The lanolin used by us, however, was free of phosphorus. It may be of more than passing interest that the sebum from dermoid cysts contained squalene but only negligible traces of "ischolesterol" (0.17, 0.02, and 0.07 per cent), using the method of Lederer and Kiun (2), while our lanolin was free of squalene and did contain "ischolesterol."

It is suggested elsewhere (7) that the triterpenoids of sebaceous materials may play some role in carcinogenesis or anticarcinogenesis.

SUMMARY AND CONCLUSIONS

1. Human sebum, as a vehicle for methylcholanthrene, is similar to lard filtrate.
2. Sebaceous substances from different animal species seem to differ in relation to carcinogenesis.
3. The nature of the anticarcinogenic action of lanolin, so far, is unexplained.

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