Calcium, Copper, and Zinc in the Epidermal Carcinogenesis of Mouse and Man*

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The role of the minerals in epidermal methylcholanthrene carcinogenesis in mice has been described (1), and the integration of the chemical, physical, and histological changes has been reviewed recently by Cowdry (3).

The present study was undertaken to compare the calcium, copper, and zinc content of mouse and human epidermis with that in squamous cell carcinomas from mouse and man respectively. Previous studies have shown that these metals are low in mouse epidermis rendered hyperplastic by methylcholanthrene, and very low in a transplantable squamous cell mouse carcinoma (1). The potassium, sodium, calcium, and magnesium content of normal human epidermis has been reported (4).

EXPERIMENTAL PROCEDURE

The procedure for separating epidermis from dermis and the analytical methods for calcium, copper, and zinc have been given in previous papers (1). Because human squamous cell carcinomas of sufficient size for analysis are rare we had to be content with 5 samples, which were gathered over a rather long period of time. However, the analyses of these showed significant differences from those of normal human epidermis, and the differences were found in all specimens. The carcinomas were cleared of blood and connective tissue and only the solid pieces were used for analysis, since necrotic tissue affects considerably the calcium content (2). Calcium determinations on all samples were done in duplicate, a practice employed also for copper and zinc when sufficient tissue was available. Seven specimens of normal human epidermis were analyzed for copper and zinc, and many samples for the alkalies and alkaline earths (4).

RESULTS

The results of analyses of normal mouse and human epidermis, mouse epidermis treated with benzene or methylcholanthrene, and mouse and human squamous cell carcinomas are shown in Table I. Only calcium, copper, and zinc were determined in the squamous cell carcinomas because of the scarcity of sufficient material. Data on these three metals are of especial interest, for they are significantly altered in epidermal carcinogenesis in mice (1). The results are expressed as micrograms of metal per 100 mgm. of epidermis. The calcium content of normal mouse epidermis is nearly three times higher than that of normal human epidermis, whereas the copper content of both is nearly the same. The zinc content of mouse epidermis is more than twice that of the human. The calcium content of hyperplastic mouse epidermis is 57 per cent less than normal, but only slightly greater than that of normal human epidermis. Also a comparison of hyperplastic mouse epidermis with normal human epidermis shows that the magnesium content of both is fairly similar, whereas the potassium and sodium content of the former is respectively about 6 and 13 per cent higher than that of the latter. In other words, methylcholanthrene-treated mouse epidermis and normal human epidermis are closely similar chemically as far as these metals are concerned. They are also somewhat alike histologically.

The calcium, zinc, and copper content of transplantable squamous cell carcinomas of the mouse induced by methylcholanthrene is respectively 80, 67, and 83 per cent less than that of untreated mouse epi-

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Table 1: Mineral Composition of Epidermis

<table>
<thead>
<tr>
<th>Material</th>
<th>K</th>
<th>Na</th>
<th>Ca</th>
<th>Mg</th>
<th>Zn</th>
<th>Cu</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>347</td>
<td>168</td>
<td>44.0</td>
<td>19.0</td>
<td>5.2</td>
<td>0.58</td>
</tr>
<tr>
<td>Benzene-treated</td>
<td>351</td>
<td>163</td>
<td>42.0</td>
<td>19.0</td>
<td>5.5</td>
<td>0.58</td>
</tr>
<tr>
<td>Hyperplastic</td>
<td>346</td>
<td>141</td>
<td>19.0</td>
<td>22.6</td>
<td>3.8</td>
<td>0.33</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>326</td>
<td>141</td>
<td>9.0</td>
<td>18.0</td>
<td>1.7</td>
<td>0.10</td>
</tr>
</tbody>
</table>

| Normal       | 322| 123| 16.0| 18.0| 2.4 | 0.54|
| Carcinoma    | .  | .  | 8.5 | .   | 1.7 | 0.16|
Carruthers and Suntzeff—Certain Minerals in Skin Carcinogenesis

Fig. 1.—Calcium, zinc, and copper in epidermal carcinogenesis in mouse and man. The data are plotted on semi-logarithmic paper, and the letters denote the following: MN—normal mouse epidermis; MH—hyperplastic mouse epidermis; MC—mouse transplantable squamous cell carcinoma; HN—normal human epidermis; HC—human squamous cell carcinoma.

dermis. On the other hand, the calcium, zinc, and copper content of human squamous cell carcinomas is respectively 47, 30, and 70 per cent less than that of normal human epidermis. Except for the pronounced decrease in copper, the diminution in calcium and zinc is not nearly so great as in the mouse carcinoma, although the amount of calcium is nearly the same in both. The possible implications of the changes in these metals during epidermal carcinogenesis in mice have been discussed (1).

The conspicuous alterations in calcium, copper, and zinc in carcinogenesis in mouse and man is more clearly illustrated in Fig. 1. These results show that the changes in these metals in the epidermal carcinogenesis of mouse and man are similar.

SUMMARY

The change in concentration of calcium, copper, and zinc in epidermal carcinogenesis in mouse and man is briefly outlined. These studies indicate that the process occurring in both species is similar, in that there are considerable decreases in the amounts of these metals when normal mouse epidermis is transformed into squamous cell carcinoma by methylcholanthrene, and when the content of these metals in normal human epidermis and in human squamous cell carcinomas is compared.

REFERENCES

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