The Morphology and Growth Characteristics of Radiation-induced Epithelial Skin Tumors in the Rat

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SUMMARY

The histology of radiation-induced epithelial skin tumors in the albino rat is described in terms of various types of nondifferentiated, sebaceous, and keratinized tumors. The frequency distribution, growth rate, and time of onset of these tumors are shown to be related to the magnitude of residual skin damage. Tumors are shown to form periodically with peak rates in the domain of 20, 40, and 60 weeks after irradiation. Evidence is presented which suggests that the structure of skin tumors is explained in terms of their origin from atrophic follicles.

INTRODUCTION

Previous papers from this laboratory described the results of a series of skin tumorigenesis experiments on albino rats involving single exposures to graded doses of $^{91}$Y beta rays, monoenergetic electrons, and alpha particles (1, 2, 4, 6). These experiments were done to evaluate the tumorigenic action of various surface and depth-dose distributions and the association between chronic radiation damage of the skin and tumor induction.

TUMOR MORPHOLOGY

The purpose of this paper is to present additional data from these experiments in order to describe the morphology, growth rates, and periodic appearance of the skin tumors, particularly as they relate to the magnitude of chronic skin damage, and the possible origin of some of the tumors from remnant hair follicles.

MATERIALS AND METHODS

The 740 histologically examined tumors used in this analysis were produced in 6 experiments. Table 1 shows the physical characteristics of the ionizing radiations used in each experiment and the number of tumors obtained from each treatment group. All of the irradiated animals were male albino rats obtained from Sprague-Dawley in Experiment 1 and Charles River (CD strain) in all of the other experiments.

The $^{91}$Y beta ray, electron, and alpha irradiation technics and dosimetric methods have been described previously (1, 2, 4, 6). Except for Experiment 1, where no anesthesia was used, the rats were anesthetized with chlorpromazine and pentobarbital and given a single radiation exposure to the skin of the back. The animals were examined frequently during the first two post-exposure months for acute skin damage and then were examined and photographed about every 4 weeks until the end of the experiment, which in most cases was 70–80 weeks. Tumor diameters were usually obtained by direct measurement of the lesions; however, when tumors were irregular in shape, the projected areas were determined planimetrically from photographs made at the time of examinations. All tumors were taken for histologic examination. Sections were stained routinely with hematoxylin and eosin. Whole skin mounts were also used for demonstrating the early appearance of skin tumors. The preparation of whole skin mounts involved separation of the epidermis and attached hair follicles from the dermis after trypsinization (3). The epidermis with attached hair follicles was stained with hematoxylin and sudan III and mounted in Kaiser's glycerol jelly on glass slides.

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TUMOR MORPHOLOGY

About 75% of the tumors were found to be endophytic, either invading the dermis (Fig. 1) or occasionally growing along the skin surface (Fig. 2); 15% of the tumors were exophytic (Fig. 3) and about 10% were observed as intradermal nodules without any connection to the surface on serial section (Fig. 4). More than 10% of the tumors undoubtedly originated within the dermis because a substantial proportion of the tumors first appeared on gross examination as intradermal nodules beneath an intact epidermis; enlarging intradermal nodules eventually ruptured through the surface epithelium and were then regarded as endophytic.

Skin tumors were classified on the basis of their differentiation patterns into 3 principle categories: keratin, sebaceous, and nondifferentiated tumors. These categories are abbreviated as K, S, and N tumors respectively. Subtypes were established within each of the 3 categories when more than a half dozen structurally similar lesions were encountered, i.e., K-1, K-2,
**Rat Skin Tumor Morphology**

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Type of radiation</th>
<th>Penetration second</th>
<th>Age at radiation (wk.)</th>
<th>Date of radiation</th>
<th>Total no. of tumors</th>
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<tr>
<td>1</td>
<td>91Y Beta</td>
<td>0.7</td>
<td>21–25</td>
<td>Dec. 1–Jan. 9</td>
<td>161</td>
</tr>
<tr>
<td>6</td>
<td>Electron</td>
<td>1.4</td>
<td>8</td>
<td>Sept. 17</td>
<td>178</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Electron</td>
<td>1.6</td>
<td>8</td>
<td>Dec. 9</td>
<td>202</td>
</tr>
<tr>
<td>9</td>
<td>Alpha</td>
<td>1.0</td>
<td>8</td>
<td>Aug. 28</td>
<td>85</td>
</tr>
<tr>
<td>10</td>
<td>Electron</td>
<td>1.0</td>
<td>9</td>
<td>Sept. 1</td>
<td>75</td>
</tr>
<tr>
<td>15</td>
<td>Alpha</td>
<td>1.0</td>
<td>8</td>
<td>Sept. 9</td>
<td>39</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>740</td>
</tr>
</tbody>
</table>

Radiation characteristics and tumor yields for each of 6 experiments.

*Expressed as half-value layer for beta rays and the maximum depth of penetration for the approximately linear depth-dose electron and alpha irradiations.

etc. The tumors were also subclassified on the basis of the predominant mode of growth as exophytic, endophytic, and subepidermal lesions. Tumors were considered exophytic when more than three quarters of the cross sectional area was above the skin surface.

**Nondifferentiated Tumors**

There were two types of nondifferentiated tumors. Ninety percent of the tumors were classified as N-1 tumors; this conformed to the descriptions by Howell for rodent cell basal epitheliomas (8) and by Zackheim for basal cell carcinoma (12). They were composed of tightly packed lobules of cells with oval or spindle-shaped nuclei and scanty cytoplasm. The histology of the tumors was the same, as shown in Figs. 5 and 6, regardless of whether they were subepidermal or endophytic. Large lesions tended to develop centrilobular necrosis. About 10% of the nondifferentiated tumors were the second type, N-2, characterized by cells with clear nonreticulated cytoplasm and small rounded nuclei (Figs. 7, 8). Nondifferentiated tumors almost never occurred in exophytic form, and about 20% were found as subepidermal nodules.

**Keratinized Tumors**

There were 3 principle types of keratinized tumors. K-1 tumors accounted for 8% of the keratinized tumors and were almost identical to nondifferentiated tumors except for the occasional presence of small foci of keratinization (Figs. 9, 10).

K-2 accounted for 23% of the keratinized tumors. In these lesions, keratinization occurred in a substantial proportion but not all of the cell lobules, and tended to form discrete spherical nodules within rounded tumor lobules (Figs. 11, 12).

K-3 tumors accounted for about 68% of keratinized tumors and were typical epidermoid lesions, i.e., squamous papillomas (Fig. 3) and squamous carcinomas (Figs. 1, 13). Fifty-seven percent of the K-3 tumors were exophytic.

In common with the nondifferentiated tumors, none of the K-1 or K-2 tumors occurred as exophytic growths; unlike the nondifferentiated tumors, K-1 and K-2 tumors were not seen as subepidermal nodules.

**Sebaceous Tumors**

There were two types of sebaceous tumors. Type S-1 was characterized by the presence of sebaceous cells in the periphery and keratinized cells in the core of the tumor pegs (Figs. 14, 15). The differentiation patterns of the exophytic and endophytic S-1 tumors were identical. Seventy percent of these tumors grew in the endophytic mode; none were observed as subepidermal nodules.

S-2 lesions were cystic in character resembling the human sebaceous cystadenoma (Fig. 16). About half of the S-2 tumors were subepidermal.

**FREQUENCY DISTRIBUTION OF THE COMMON TUMOR TYPES**

Table 2 shows the percentage distribution of the major tumor types for the indicated dose groups in each of 6 experiments. Approximately three-quarters of the tumors could be accounted for in equal proportions by three kinds of tumors: K-3, S-1, and N.

In Experiments 1, 6, 9, and 10, for electron and alpha penetrations ~1.0 mm, or 91Y beta rays which had the equivalent penetration, there was a sufficient range of treatment groups to demonstrate a definite dependence of tumor type on radiation dose. There was a predominance of keratin Type-3 tumors at high doses and a preponderance of nondifferentiated tumors at low doses. However, the depth of penetration and the type of radiation affected the relationship between dose level and the distribution of tumor types. For example, in Experiment 6, a dose of 6200 rads of electrons, which penetrated only 0.4 mm, produced the same distribution of tumor types as that which occurred with deeper irradiations at a
much lower surface dose. A comparison of Experiments 9 and 10 shows that the shift to a predominance of keratinizing tumors occurred at a lower dose with alpha radiation compared to electron radiation.

The effects of penetration depth and type of radiation could be eliminated by relating the distribution of tumor types to the magnitude of residual skin damage as indicated for each dose group in Table 2. Damage-Category 4 was the maximum form of injury; it was characterized by the presence of a narrow, white, hairless scar resulting from very severe acute ulceration. Damage-Category 3 was characterized by a moderately contracted partially epilated scar. In Damage-Category 2, there was minimal shrinkage of the irradiated area, but partial epilation was present; the epidermis was also white due to loss of the brown surface scale normally present on male albino rats. Damage-Category 1 was characterized by patchy areas of whitened epidermis as the only abnormality.

Table 3 groups the tumor types according to the degree of injury. The maximum tumor yield, or about 60% of all tumors, occurred with Grade 2 damage. A pronounced dependence on the grade of damage is shown by 2 of the tumor types, K-3 and N. K-3 tumors predominated at Grade 4 damage but decreased in relative numbers at lesser grades of injury. The nondifferentiated tumors showed the opposite relationship to chronic injury. The relative frequency of S-1 tumors was not affected by the degree of chronic damage. S-2 tumors accounted for a significant proportion of the total tumor yield only at Grade 1 damage.

Multiple tumor formation on individual rats occurred particularly at Grade 2 and 3 injury (Table 3). There was a random distribution of the number of tumors occurring on individual rats (4). There was no stratification of tumors according to type on individual rats.

GROWTH RATE AND TUMOR TYPE

Skin tumors in the rat display a variety of growth patterns, as shown in Chart 1. Some were indolent, remaining at a di-

<table>
<thead>
<tr>
<th>Dose (rads)</th>
<th>Initial no. of rats</th>
<th>Skin damage grade</th>
<th>No. of tumors</th>
<th>Tumor type (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>N  K-1 K-2 K-3 S-1 S-2 Other</td>
</tr>
<tr>
<td>Experiment 1 (91Y beta)</td>
<td>8,600</td>
<td>24 4 25</td>
<td>8 0 4 72 16 0 0</td>
<td></td>
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<tr>
<td>4,870</td>
<td>13 3 30</td>
<td>27 0 10 33 27 0 3</td>
<td></td>
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<tr>
<td>3,125</td>
<td>29 2 92</td>
<td>39 2 9 22 20 5 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1,020</td>
<td>48 1 14</td>
<td>7 21 14 0 8 36 14</td>
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<td></td>
</tr>
<tr>
<td>Total</td>
<td>114 161</td>
<td>29 3 9 30 20 6 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experiment 6 (e-, 1.4-mm penetration)</td>
<td>5,000</td>
<td>33 4 28</td>
<td>14 0 0 36 39 0 11</td>
<td></td>
</tr>
<tr>
<td>2,000</td>
<td>18 2 53</td>
<td>50 8 4 15 21 2 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>51 81</td>
<td>38 5 2 22 27 1 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experiment 6 (e-, 0.7-mm penetration)</td>
<td>3,000</td>
<td>32 2 57</td>
<td>30 2 5 23 35 4 1</td>
<td></td>
</tr>
<tr>
<td>6,200</td>
<td>32 1 40</td>
<td>45 3 10 5 25 8 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experiment 7 (e-, 1.4-mm penetration)</td>
<td>2,300</td>
<td>32 3 65</td>
<td>35 0 8 29 20 2 6</td>
<td></td>
</tr>
<tr>
<td>1,700</td>
<td>33 2 137</td>
<td>30 1 12 18 33 1 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>65 202</td>
<td>32 1 11 22 29 2 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experiment 9 (alpha, 1.0-mm penetration)</td>
<td>2,360–6,850</td>
<td>35 4 19</td>
<td>5 0 5 68 11 5 5</td>
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<td>1,050–1,580</td>
<td>20 3 24</td>
<td>25 0 25 25 25 0 0</td>
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<td>710</td>
<td>10 2 30</td>
<td>37 3 7 37 17 0 0</td>
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<tr>
<td>210–480</td>
<td>17 1 12</td>
<td>58 8 0 0 24 8 0</td>
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<td></td>
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<tr>
<td>Total</td>
<td>82 85</td>
<td>29 2 10 35 18 2 1</td>
<td></td>
<td></td>
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<tr>
<td>Experiment 15 (alpha, 1.0-mm penetration)</td>
<td>710–1,000</td>
<td>24 2 39</td>
<td>23 18 13 28 18 0 0</td>
<td></td>
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<tr>
<td>Experiment 10 (e-, 1.0-mm penetration)</td>
<td>10,225</td>
<td>19 4 10</td>
<td>10 0 0 70 20 0 0</td>
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<tr>
<td>5,535</td>
<td>16 3 22</td>
<td>23 0 5 45 27 0 0</td>
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<tr>
<td>2,400</td>
<td>16 2 43</td>
<td>35 5 16 16 28 0 0</td>
<td></td>
<td></td>
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<tr>
<td>Total</td>
<td>51 75</td>
<td>28 3 11 32 27 0 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grand total</td>
<td>451 740</td>
<td>31 3 11 26 25 3 3</td>
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<td></td>
</tr>
</tbody>
</table>

The percentage distribution of tumor types according to dose for each of 6 experiments.
The median diameter for tumors, regardless of type, was 4.8 mm; there was a very broad distribution as indicated by the geometric standard deviation of 3.2. Nondifferentiated tumors were average in growth rate; keratinized tumors were somewhat larger than average, while the opposite was true for sebaceous tumors.

Chart 3 shows the size frequency distribution of tumors with respect to grade of skin damage and demonstrates that tumors forming in radiation scars (Grade 4) were somewhat larger than those developing at lower levels of injury. This is due in part to the predominance, at Grade 4 damage, of K-3 tumors which tended to be above average in size. However, the growth rate of K-3 tumors forming in radiation scars (Grade 4 damage) was twice as fast as the same tumor type developing in skin with Grade 2 injury.

Because of these variable patterns, growth rate was measured in terms of tumor diameter 20 weeks from initial appearance. Tumor onset was taken to be the time when a lesion reached a diameter of 1–2 mm. The growth period of 20 weeks afforded a relatively long observation period without eliminating an excessive number of tumors from the analysis of growth characteristics.

The cumulative frequency distribution of 488 tumor diameters after 20 weeks of growth is shown in Chart 2 for tumors of all types as well as for K, S-1, and N tumors. It is evident that the frequency distribution of tumor growth rates is consistent with a log-probability distribution. The median diameter for tumors, regardless of type, was 4.8 mm; there was a very broad distribution as indicated by the geometric standard deviation of 3.2. Nondifferentiated tumors were average in growth rate; keratinized tumors were somewhat larger than average, while the opposite was true for sebaceous tumors.

Table 3

<table>
<thead>
<tr>
<th>Skin damage</th>
<th>Initial no. of rats</th>
<th>No. of tumors</th>
<th>Tumor type (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>N&lt;br&gt;</td>
</tr>
<tr>
<td>4</td>
<td>111</td>
<td>82</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>81</td>
<td>141</td>
<td>28</td>
</tr>
<tr>
<td>2</td>
<td>162</td>
<td>451</td>
<td>39</td>
</tr>
<tr>
<td>1</td>
<td>97</td>
<td>66</td>
<td>47</td>
</tr>
</tbody>
</table>

The percentage distribution of tumor types according to grade of skin damage.

Includes K-1 tumors.
PERIODIC APPEARANCE OF TUMORS

Tumor formation rates were calculated as the number of new tumors per surviving rat per week during the interval between each successive examination. Chart 4 shows the tumor formation rates for each of the 4 dose groups in Experiment 1 and demonstrates a periodicity to the appearance of new tumors at all doses. Peak rates occurred at about 20, 40, and 60 weeks.

Chart 5 shows the tumor formation rates for the optimal tumorigenic dose levels in Experiments 7, 9, 10, and 15. The tumor formation rates are presented as running averages to emphasize the major peaks. It is evident that there is a substantial degree of similarity amongst all the experiments in that they show a distinct periodicity to the appearance of new tumors with peak rates occurring in the domain of 20, 40, and 60 weeks, However, there was an earlier second peak in Experiment 15 and what might be regarded as a split third peak at 55 and 65 weeks in Experiment 10.

The relative magnitudes of the individual peak tumor formation rates were somewhat dose-dependent. This is illustrated in Experiment 1 (Chart 4) where the 40- and 60-week peaks were most prominent at or below the optimum tumorigenic dose of 3125 rads, while at the two higher doses, a larger proportion of the tumors formed before 40 weeks. Relatively early tumor formation in Grade 4 skin damage was also seen in the other three experiments that had a sufficient range of exposure to make this comparison possible (Experiments 6, 9, 10).

Some stratification in the time of appearance with respect to tumor type was observed. The early-appearing endophytic K-3...
tumors and late-appearing nondifferentiated tumors showed
the greatest contrast, as illustrated in Chart 6, for the optimum
tumorigenic dose in Experiment 7. Sebaceous tumors occurred
more uniformly in time than the endophytic K-3 or nondif-
ferentiated tumors.

DISCUSSION

The classification scheme used here was developed because
of the need for an explicit and simple nomenclature. The lack
of general acceptance of any of the various classification
schemes proposed for human skin tumors has been described
by Lund (5). The ambiguities in the nomenclature used for
radiation and chemically induced skin tumors in the rat have
also been described (8, 12). In spite of the differences in termin-
ology, the same kinds of skin tumors were observed in these
experiments as those described for the rat by Howell (8) in
response to the chemical carcinogens, methylcholanthrene
(MC) and 9,10-dimethyl-1,2-benzanthracene (DMBA) and by
Zackheim (10—12) in response to MC, DMBA, grenz, and
X-rays.

The data presented in this paper demonstrate that the fre-
quency distribution of tumor types is related to the magnitude
of residual skin damage with N, K-1, and K-2 tumors, tending
to disappear at pilocidal doses. An analogous relationship may
occur with skin tumors produced in the rat by chemical carcin-
ogens. DMBA produces relatively severe skin injury and a pre-
dominance of squamous tumors, while MC, which cause less
injury, produces a predominance of other forms of epithelial
skin tumors, presumably of hair follicle origin (8, 11, 12).

Other reports from this laboratory describe the strong associ-
ation between residual hair follicle damage in the form of
atrophic hair follicles and tumor formation (3, 6). Figures 17
and 18 show the appearance of normal and atrophic hair folli-
cles respectively on whole skin mounts. Parallel dose-incidence
curves for tumors and atrophic follicles were observed under a
wide range of conditions which affected the tumor yield (3, 6,
7): where there was a shift in the tumorigenic action of
ionizing radiation by change in the spatial distribution (i.e.,
varying the penetration depth of electrons or irradiating in a
slieve instead of a uniform surface pattern) or by changing the
type of irradiation (alpha instead of electron irradiation), there
was a parallel shift in the yield of atrophic follicles with a
relatively stable ratio of tumors to atrophic follicles of 1 per
2000.

A plausible explanation for the constant association between
tumors and atrophic follicles is that most skin tumors develop
from atrophic follicles. This mode of tumor formation is sup-
ported by the occurrence of lobulated growths, resembling
microtumors, on atrophic hair follicles (Fig. 19).

The origin of skin tumors from atrophic follicles would
imply that the two types of lesions have morphologic similar-
ities because, in general, the structure of tumors tends to re-
semble the tissue of origin. There is some histologic evidence
that the structure of some of the principle tumor types can be
explained by the character of the atrophic follicles. A common
form of follicle atrophy resembling the neck and sebaceous
gland of a resting hair follicle is shown in Fig. 20. The develop-
ment of an S-2 tumor from this type of abnormality is sug-
gested by Fig. 21.

Nondifferentiated tumors frequently appear subepidermally
(Fig. 4) and virtually disappear with irradiations that cause
Grade 4 damage (i.e., epilated scars). Subepidermal nests of
nondifferentiated cells are frequently seen in serial sections of
irradiated skin with moderate damage (Fig. 22) but not in the
contracted scars of Grade 4 damage.

Another type of atrophic follicle which suggests the develop-
ment of the S-1 tumor, illustrated in Fig. 15, is shown in Fig.
23, which consists of a remnant follicle stalk with keratiniza-
tion in its core and sebaceous cells along its outer surface. K-3
tumors presumably arise either from the surface epidermis it-
self or from nonsebaceous remnant follicle stumps which oc-
cur most commonly at the highest grades of damage, i.e.,
where the K-3 tumors predominate.

The periodic appearance of new skin tumors, at about 20,
40, and 60 weeks in each of six experiments, suggests that
there is some type of generalized periodic stimulation to the
formation of skin tumors. Cyclic growth of hair may be re-
lated to this growth stimulation. The concordance of growth
spurts in mouse skin tumors with passing waves of hair growth
has been reported (5). However, the hair growth pattern of
mature rats is not well characterized beyond the observation
that it occurs in a patchy fashion.

The evidence for the origin of skin tumors from atrophic
follicles in response to periodic growth stimulation suggests
that the dominant pathogenic mechanism for tumor formation
is the structural derangement of the skin. The log-probability
It E. Albert, M. E. Phillips, P. Bennett, F. Burns, and R. Heimbach

distribution of tumor growth rates (i.e., the lack of discrete populations of "benign" and "malignant" tumors) suggests that the magnitude of structural responses of remnant hair follicles to growth stimulation may depend on local conditions in the skin, e.g., the character of the local vasculature. Radiation-induced enrichment of the vascular bed is particularly striking in radiation scars (Fig. 24) where there is the relatively rapid growth of the few tumors that do occur. Similar vascular abnormalities, but of a focal nature, also occur in the absence of tumors in Grade 2 damage (Fig. 25).

REFERENCES


Figs. 1—16 and 20—23. Stained with hematoxylin and eosin. Figs. 17—19. Whole-mount preparations of the surface epidermis and hair follicles, stained with hematoxylin and sudan III.
Fig. 1. Endophytic keratin Type-3 tumor. × 25.
Fig. 2. Keratin Type-1 tumor growing along the skin surface. × 25.
Fig. 3. Exophytic keratin Type-3 tumor. × 25.
Fig. 4. An intradermal nondifferentiated Type-1 tumor nodule. × 25.
Fig. 5. Nondifferentiated subepidermal Type-1 tumor. × 450.
Fig. 6. Nondifferentiated endophytic Type-1 tumor with growth pattern as in Fig. 2. × 450.
Fig. 7. Nondifferentiated Type-2 tumor. × 100.
Fig. 8. Nondifferentiated Type-2 tumor showing clear cells. × 250.
Fig. 9. Keratin Type-1 tumor. × 100.
Fig. 10. Keratin Type-1 tumor. × 450.
Fig. 11. Keratin Type-2 tumor. × 25.
Fig. 12. Keratin Type-2 tumor. × 100.
Fig. 13. Endophytic keratin Type-3 tumor. × 100.
Fig. 14. Exophytic sebaceous Type-1 tumor. × 25.
Fig. 15. Exophytic sebaceous Type-1 tumor. × 100.
Fig. 16. Sebaceous Type-2 tumor. × 25.
Fig. 17. Whole-mount preparation of normal hair follicles. × 15.
Fig. 18. Whole-mount preparation at optimum tumorigenic dose in Experiment 7, showing atrophic follicles and microtumors indicated by the arrows. × 15.
Fig. 19. Microtumors forming from the base of atrophic hair follicles on a whole skin mount preparation. × 25.
Fig. 20. Follicle remnant resembling neck of follicle with sebaceous gland at lower end. × 25.
Fig. 21. Formation of an S-2 tumor from base of remnant hair follicles. × 25.
Fig. 22. Isolated epithelial nest (arrow) in the dermis with overlying follicle remnant attached to skin surface. × 25.
Fig. 23. Atrophic follicle forming S-1 tumor. × 25.
Fig. 24. Dermal vasculature perfused with India ink, showing the overgrown vascular bed of one-half of a contracted radiation scar. The epidermis and hair follicles were removed after trypinization. The dermis was cleared in methylsalycilate. × 25.
Fig. 25. Perfused dermal vasculature (as in Fig. 24) in a skin with Grade 2 damage showing a focal vascular overgrowth. × 40.
Rat Skin Tumor Morphology

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The Morphology and Growth Characteristics of Radiation-induced Epithelial Skin Tumors in the Rat


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