Squamous-cell carcinomas, hemangiomas, fibromas, and papillomas have occurred in the skin of ducks following the local application of a 0.25 per cent acetone solution of methylcholanthrene daily for a period of 1 month (5, 6). The spontaneous disappearance of a high per cent of these neoplasms in the duck has proved to be a feature of considerable interest (7). Attempts have been made infrequently to produce neoplasms in fowls by the local application of carcinogens to the skin. Hartwell (2), in 1951, cited four experiments in which the skin of fowls was treated with 3,4-benzpyrene. In one the skin of pigeons was used, and one spinocellular epithelial neoplasm developed. In three experiments the skin of fifteen chickens was treated, and one bird developed an epithelioma.

The spontaneous occurrence of carcinomas in the skin of fowls is apparently infrequent. Olson and Bullis (4) reported one case of a squamous cell carcinoma in the skin of a chicken. Feldman and Olson (1), in 1944, cited only a few previously reported cases in their study of neoplastic diseases in chickens. These authors stated "In the cases we have observed the neoplasms have remained localized, and in the cases reported previously by others, metastasis has rarely been demonstrated."

In this study methylcholanthrene was applied to the skin of chickens, and squamous-cell carcinomas developed.

METHODS AND MATERIALS

The chickens were 2-day-old Rhode Island Reds obtained from a commercial hatchery. They were kept for 42 days in the laboratory, at which time a 0.25 per cent solution of methylcholanthrene in acetone was first applied locally to the skin beneath the right wing of eighteen chickens. This carcinogen was applied daily for 1 month thereafter. It was dropped onto the skin, and approximately 1–2 ml. was used daily per bird. Acetone was applied in a similar manner to six control chickens.

All chickens were kept in a battery and observed frequently. Chick Startena and Growena (Purina) and water were available ad libitum. The neoplasms that developed in the treated areas of skin were observed macroscopically, and many were photographed at intervals. Some of the lesions were excised for histological study; they were fixed in a 4.0 per cent solution of formaldehyde. Paraffin sections were prepared and stained routinely with hematoxylin and phloxine. A few of the chickens with tumors were sacrificed and autopsied. This material was also studied histologically. The majority of the neoplasms were allowed to regress completely, and the birds were then sacrificed and autopsied.

RESULTS

Six chickens did not show any gross changes in the skin and were discarded on the 86th day following the last application of acetone. During the time the chickens were treated with the acetone solution of methylcholanthrene, a few developed local areas of ulceration. The methylcholanthrene was discontinued for several days. These ulcerated areas completely healed within 30 days, and the feathers continued to grow.

Eight of the eighteen methylcholanthrene-treated chickens did not develop any neoplasms and were discarded on the 86th day after the last application of the carcinogen. Approximately 60 days after administration of the carcinogenic agent was discontinued, papillomas and focal areas of ulceration began to appear in the treated areas of skin. These lesions continued to appear for an additional 40 days. One chicken, however, developed new lesions in the treated areas of skin 5 months after the last application of methylcholanthrene. The papillomas were usually small. Histologically, they showed the typical characteristics of such a lesion. The focal areas of ulceration...
tion were usually round or oval, their margins were slightly indurated, and the base was granular. They varied in size from 0.5 to 1.5 cm. (Fig. 1). Five such lesions on four different chickens were removed for histological study. One chicken, #589, with six tumors was also sacrificed, and the lesions were studied histologically. The base of these ulcers showed a wide zone of squamous epithelial cells (Figs. 3, 4, and 5). Intercellular bridges and epithelial pearls were present (Figs. 4, 7, and 10). The epithelial cells varied widely in size and shape, as well as in their staining reaction (Figs. 8 and 9). In some of these ulcers extensive degenerative changes had occurred, while in others the tumor cells were well preserved. Necrosis and leukocytic infiltration were conspicuous in some of the lesions. Usually, these ulcers were also infiltrated with a large number of mononuclear cells that resembled lymphocytes and plasma cells. Large groups of lymphocyte-like cells were present about the base of some of these carcinomatous ulcers (Figs. 3 and 7).

Five chickens had from one to three ulcerated areas, varying in size from 0.5 to 1.5 cm. in diameter and 1 to 3 mm. in depth. Each lesion progressively healed spontaneously within 20–60 days. When these chickens were sacrificed 1–2 months later, there was no evidence of either local recurrence or metastasis.

Three chickens developed typical papillomas. One was removed, and it had the characteristic microscopic features of such a tumor. Usually only one or two papillomas occurred in a single bird. They were small—3–5 mm. in diameter. Only one reached a height of 1.0 cm. These papillomas ultimately disappeared spontaneously. Three chickens had several papillary-like lesions in the skin that could not be diagnosed grossly as either a benign or malignant lesion. These also spontaneously regressed.

The process of spontaneous regression of these ulcerated lesions is shown in Figures 1 and 2. Grossly, these regressing lesions were identical with those ulcers removed and showed the histological features consistent with the diagnosis of squamous-cell carcinoma. The rate of regression varied. Some completely regressed within a period of 3 weeks, while others slowly regressed over a period of 6 weeks.

**DISCUSSION**

The skin of five chickens from the group of eighteen treated daily for 30 days with a 0.25 per cent solution of methylcholanthrene developed one or more ulcerative lesions that showed histologically the characteristics of a squamous-cell carcinoma. No metastasis occurred. Five other chickens with similar lesions had a complete and spontaneous regression of the lesion. The mechanism by which this regression occurs is unknown. It is of interest, however, to observe the extensive degeneration of the epithelial cells and to note the accumulation of reticuloendothelial cells in and about the periphery of these neoplasms. Whether this cellular response is "cause or effect" is difficult to state at this time. It is of interest to find a similar cellular reaction about squamous-cell carcinomas and hemangiomas in the skin of white Pekin ducks treated with methylcholanthrene that likewise spontaneously regressed (5, 7). A similar cellular reaction has been observed in the spontaneously developing and regressing hemangiomas in chickens (8).

Some may question the diagnosis of squamous-cell carcinomas in these chickens, since none of the tumors metastasized and all spontaneously regressed. Histologically, these tumors, in our opinion, have all the characteristics of a malignant neoplasm, as shown in the group of illustrations. We do not think that these squamous cells

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**Fig. 1.**—Chicken #620. Two typical squamous-cell carcinomas are shown on the wing. Photograph made on 86th day following last application of methylcholanthrene to skin.

**Fig. 2.**—Chicken #620. One of ulcers has completely healed, while the second has almost completely regressed. Photograph made 60 days after that shown in Figure 1.

**Fig. 3.**—Chicken #584. Base of the ulcer is diffusely infiltrated with squamous epithelial cells. Tumor removed on 180th day after methylcholanthrene discontinued. H&P X 90.

**Fig. 4.**—Chicken #584. Epithelial pearls are frequently found in the base of these ulcers. H&P X 150.

**Fig. 5.**—Chicken #620. There is a wide zone of epithelial cells forming the base of this ulcer. A few leukocytes are present on the surface. H&P X 90.

**Fig. 6.**—Same as Figure 5. H&P X 150.
Fig. 7.—Chicken #584. Squamous cells and epithelia pearls are present in base of this ulcer. Note their extension into adjacent fatty stroma. Frequently lymphocytes are present at base of these neoplastic lesions. H&P × 140.

Fig. 8.—Chicken #620. This tumor is characterized by sheets of epithelial cells extending down into the underlying stroma. H&P × 140.

Fig. 9.—Chicken #620. Variations in size, shape, and staining reaction occur in these tumor cells. Mitotic cells are frequent. H&P × 855.

Fig. 10.—Chicken #620. Some of the squamous epithelial cells show intercellular bridges. H&P × 1425.
at the base of the lesion represent a pseudo-epi-
theiliomatous hyperplasia. They are interesting
in view of the studies of Rous and associates (3,
9) with tarring of rabbits. These investigators ob-
served that “tarring itself will provide the needed
encouragement, but when it is left off the growths
disappear unless other factors act to maintain
them, as e.g. chronic pathological changes in the
supporting tissue, or inflammation due to bac-
terial infection or to crowding” (3). These tumors
in the chicken followed by several weeks the last
application of methylcholanthrene, and appear-
tly the only injury that might have occurred would
have been the plucking of feathers. In these neo-
plastic lesions in the chicken there were no macro-
scopic changes to suggest a preceding benign type
of lesion, such as has been described in rabbits
(9). Rous and Kidd (9) state “When the chemical
agents commonly termed carcinogenic are applied
to the skin of man, the rabbit, or the mouse, they
nearly always elicit benign growths some while
before cancer appears, and the latter frequently
takes origin from one or another of them.” Could
it be that a neoplastic growth, such as these in
the chicken, requires some “factor” to keep the
cells progressively developing, while the absence
of such a “factor” results in spontaneous regres-
sion of the growth?

It is of interest to find that methylcholanthrene,
when applied locally to the skin of young Rhode
Island Red chickens, produces primarily a squa-
mos-cell carcinoma, while the same carcinogen
applied to the skin of white Pekin ducks produces
primarily hemangiomas. The absence of a lym-
phatic system in the skin of fowls, like that in
mammals, may be a significant factor affecting
the development, regression, and spread of malig-
nant tumors.

SUMMARY

A histological squamous-cell carcinoma oc-
curred in the skin of five chickens in a group of
eighteen treated with an acetone solution of
methylcholanthrene. Five other chickens, similar-
ly treated, developed one or more ulcerative les-
ions macroscopically identical to those studied
histologically and referred to above. These latter
lesions spontaneously regressed within a period
of 2–8 weeks.

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