Autoradiographic Evidence of Cortisone Action on Mast Cells in Experimental Skin Tumors*

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Chemical (10, 11, 17), histochemical (3, 10–12, 15), and autoradiographic (5) studies unanimously indicate that the mast cells of the connective tissue contain a sulfate-containing mucopolysaccharide which, chemically, is closely related to heparin and hyaluronic acid (which does not contain sulfate) without being identical with either.

The author (1–4, 16) observed morphological changes in tissue mast cells following administration of ACTH and cortisone to human beings and to various experimental animals. The mast cells become degranulated, vacuolized, grow smaller, and change in shape—often to bizarre, ragged cells. The number of histologically demonstrable mast cells is reduced. These findings have been confirmed by Cavallero and associates (7, 8), Stuart (14), F. Bloom (6), and others.

During the administration of cortisone to mice given one painting of the carcinogenic hydrocarbon 9,10-dimethyl-1,2-benzanthracene, Engelbreth-Holm and Asboe-Hansen (9) observed similar morphological changes in the dermal mast cells; moreover, the mast-cell count was reduced. These changes were observed in an experimental series in which the incidence of tumors was essentially re-

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METHODS

Eight female albino mice of the strain St/Eh with well marked papillomas of 7–10 days’ standing were given intraperitoneal injections of S\(^{35}\), 8 \(\mu\)g/gm body weight with 0.1 mg of Na\(_2\)SO\(_4\) as carrier. At the end of 48 hours the mice were killed, and the tumor as well as normal skin was removed and fixed in 70 per cent alcohol. The specimens were imbedded in paraffin and cut into sections of 7 \(\mu\). Following deparaffinization and drying, the sections were studied by autoradiography according to the Pelc stripping film technic (13). The films were exposed for 17 days.

Autoradiographs of histological sections through experimental skin tumors after the uptake of radioactive sulfur.

Fig. 1.—Untreated mouse. Mag. approx. \(\times 850\). Bright field microscopy; focused on the film. Unstained preparation. Intense blackening of the film over the mast cells of the connective tissue (dark spots); fainter, diffuse blackening over the surrounding connective tissue (small dark dots).

Fig. 2.—Same preparation as Figure 1, phase contrast microscopy; focused on the tissue slide. Mag. approx. \(\times 850\). Note the deep extensions of the hyperplastic epithelium.

Fig. 3.—Untreated mouse. Mag. approx. \(\times 850\). Dark field microscopy; focused on the film. The hyperplastic epithelium at the top extends into the corium. The mast cells of the connective tissue appear as bright discs, indicating a high content of radiosulfur. The diffuse and fainter blackening over the ground substance, indicating a considerably lower content, appears as small light dots.

Fig. 4.—Cortisone-treated mouse, dark field microscopy; focused on the film. Mag. approx. \(\times 850\). Radiosulfur content of the mast cells lower, that of the surrounding connective tissue relatively high. The difference considerably equalized.
The unstained preparations were examined and photographed with bright field (Fig. 1), phase contrast (Fig. 2), and dark field microscopy (Figs. 3 and 4), focused on the film as well as on the tissue slide. Dark field microscopy exhibits the best contrast and the most exact picture of the blackening of the film provoked by the radiosulfur. Then the preparations were stained with ½ per cent aqueous solution of toluidine blue for 15 minutes.

RESULTS

A marked difference was observed between the distribution of radiosulfur in the tumors of mice treated with cortisone and of untreated mice. Monitoring with a Geiger counter showed a high content of radiosulfur in the tumors of both groups.

Over the mast cells (identified by metachromatic stain) in the connective tissue of the tumors of the untreated mice, the stripping film was intensely blackened, indicating a high radiosulfur content. Over the surrounding connective tissue the blackening was relatively fainter (Figs. 1 and 3). In the cortisone-treated mice this difference was considerably reduced: the uptake of radiosulfur in the mast cells was relatively scarce, that of the ground substance unchanged or slightly reduced (Fig. 4).

DISCUSSION

The histological observation of certain morphological changes in mast cells due to cortisone—degranulation, vacuolation, etc.—are supported by these autoradiographic observations. The mast cells evidently take up less radiosulfur during treatment with cortisone.

The difference between the specimens from untreated and cortisone-treated mice was constant in all mice. Moreover, previous experiments, with various methods of fixation (70 per cent alcohol, 10 per cent formalin, 4 per cent basic lead acetate), and freeze-drying had given uniformly similar results. It is unlikely, therefore, that the histological preparation could have produced artifacts disturbing the comparability of the specimens from the two groups.

SUMMARY

The mast cells in experimental skin tumors of mice take up ample radiosulfur, when given intraperitoneal injections of $^{35}$S with Na$_2$SO$_4$ as carrier. After 15 days' treatment with cortisone, the mast cells of the tumor connective tissue took up considerably less radiosulfur. This supports previous histological findings which indicate that, when mast cells are subjected to the action of cortisone, they lose sulfomucopolysaccharide.

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