though several compounds showed brilliant blue-violet fluorescence under ultraviolet excitation. To my knowledge, all toluene-soluble substances that exhibit fluorescence in the neighborhood of 4000 A and are not colored in this region are more or less good scintillators. Thus, we must conclude that one or more steps of the chain involved in the scintillation process cannot occur in ordinary aqueous solution. Some "shot" experiments have been made with aqueous solutions of these compounds to which additives such as inorganic ions and simple organic substances have been added. None of these gave positive results.

JAMES R. ARNOLD*
Institute for Nuclear Studies, University of Chicago, Chicago, Illinois

References and Notes

1. I wish to thank John Marshall of the Institute for Nuclear Studies for suggesting the examination of these compounds. And I also thank the companies that so generously furnished samples for their cooperation in making these measurements possible. This research was supported under a contract with the Office of Ordnance Research.
2. F. N. Hayes and R. G. Gould, *Science* 117, 480 (1953). I am indebted to Hayes for a private communication on POPOP.
* Present address: Department of Chemistry, Princeton University, Princeton, N.J.

20 July 1955

Radiosensitivity of Anoxic Skin in Relation to Temperature

Reduced temperature in mammalian skin during exposure to ionizing radiations is accompanied by reduced radiosensitivity. This is interpreted in terms of an accompanying reduction in vascular supply. The radiosensitivity-modifying effect of alterations in vascular supply is ascribed to accompanying changes in oxygen tension; in effect, the protective influence of reduced temperature is attributed to the anoxic condition that it promotes. This view is supported by the radioresistance-enhancing effect of anaerobiosis in other protoplasmic systems (*1, 2*). However, there appear to have been no studies of the effect of temperature, during irradiation, on the radiosensitivity of skin when variations in oxygen tension are simultaneously precluded. This report is concerned with this question (*3*).

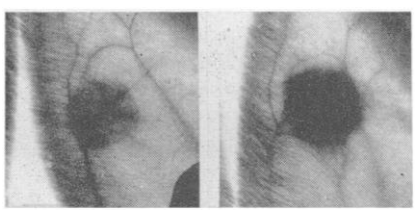

Fig. 1. Typical erythematous reaction 1 week following exposure to 28,800 r in a cooled tissue area (left) and in a warmed tissue area (right).

Homologous areas of the ears of female albino rabbits were simultaneously dehematized and conditioned to different temperatures shortly prior to and during exposure to heavy doses (up to 28,800 r) of soft x-rays (50 kv; 5 ma; 3600 r/min; beryllium window). Intensity of the erythema at 24 hours, 1 week (Fig. 1), and 2 weeks subsequent to exposure and the severity of later lesions, up to 8 weeks subsequent to exposure, were used as criteria of radiation damage. Each area was dehematized for 3 minutes prior to temperature regulation; then followed 10 minutes of combined dehematization and temperature regulation; this, in turn, was followed by 8 minutes of irradiation; the area was then released. Only a single area on any one ear was employed.

The technique is diagramed in Fig. 2. Tissue temperature was regulated by the temperature of the water flowing through the copper chamber. Dehematization was induced by compression; we employed a weight of 1140 g. Tissue temperatures were measured with a thermocouple. The beryllium compression surface insured maximum transmission of x-rays to the tissue. The dehematized area measured 218 mm^2; the irradiated area, in the center of the former, measured 95 mm^2. The fact that circulation was eliminated was demonstrated by injecting Evans blue in the artery of controls; no coloration appeared in the compressed area after this injection. Controls were effected on the opposite ear of one and the same experimental animal; in these, no untoward responses occurred.

This report is based on observations on about 30 warmed and 30 cooled tissue sites. In several instances, the radiation dose and the period of induced ischemia and temperature regulation were less than indicated; these experimental variations did not, however, essentially affect the over-all pattern of response. In general, the radiosensitivity of the anoxic tissue was found to be definitely reduced following irradiation at the lower temperature. The postirradiation responses, at various times after irradiation, of cooled (about 10°C) and warmed (about 39°C) tissue areas that were exposed to 28,800 r follow.

1) At 24 hours after irradiation: in 82 percent of the areas the intensity of the erythema was distinctly less in the cooled areas than it was in the warmed areas.

2) At 1 week after irradiation: in 88 percent of the areas the differential in erythematous response was the same as that described for 24 hours, but the contrast was decidedly greater (Fig. 1).

3) At 2 to 3 weeks after irradiation: with progressing complexity of the lesions, warmed areas continued to exhibit the more severe reaction; this was especially reflected in a corona of inflammation

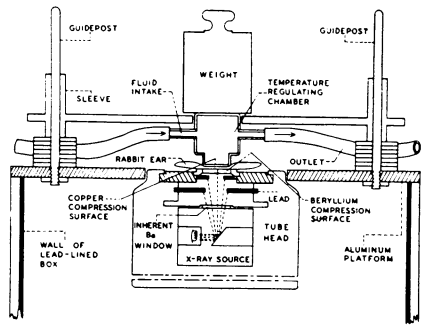

Fig. 2. Device by means of which anoxia, temperature-regulation and irradiation are simultaneously effected in localized areas of the rabbit ear.

peripheral to the irradiated area; this pattern prevailed in 90 percent of the areas.

4) At 4 to 7 weeks after irradiation: the same pattern of response continued and was evident in 96 percent of the areas. At 4 weeks, 40 percent of the warmed areas exhibited sequestration of the irradiated area (perforation); there was no sequestration in cooled areas. At 5 weeks, 83 percent of the warmed areas and 54 percent of the cooled areas exhibited sequestration. After sequestration, the corona of inflammation persisted for a considerable time in warmed areas but disappeared rapidly in cooled areas.

5) At 8 weeks after irradiation: there was total sequestration of the irradiated area in all warmed areas, and the perforation was always significantly larger than that occurring in cooled areas; 60 percent of the cooled areas exhibited perforation significantly smaller than the irradiated area; the remainder exhibited extremely small perforation or none at all.

These observations are offered as evidence, possibly the first of its kind, that the temperature prevailing in anoxic mammalian tissue at the time of irradiation is a significant dose-effect modifying factor.

J. P. O'BRIEN
E. J. FRANK
J. L. GARNER
Department of Biology, Marquette University, Milwaukee, Wisconsin

References and Notes

1. H. M. Patt, *Physiol. Revs.* 33, 35 (1953).
2. We demonstrated earlier, specificially for the rabbit ear, the respectively protective and compromising effect of cooling and warming during irradiation; we also demonstrated the protective effect of ischemia. J. P. O'Brien *et al., Anat. Record* 117, 530 (1953).
3. Work performed under U.S. Atomic Energy Commission contract No. AT(11-1)324 with Marquette University. We were aided (preliminarily) by the Milwaukee Division of the American Cancer Society. The x-ray equipment was provided by the X-Ray Department, General Electric Co. The assistance of Barbara Herbes and Phyllis Galasinski is gratefully acknowledged.

18 July 1955