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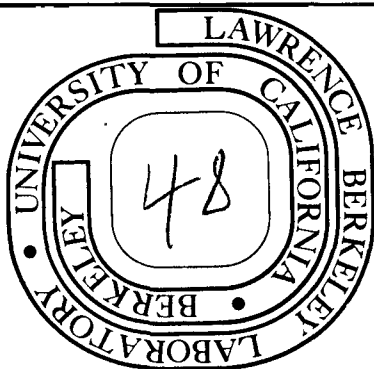
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Chapter V

Somatic Effects - Cancer

Pharynx and Hypopharynx

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I. PHARYNX AND HYPOPHARYNX

The 1972 NAS-BEIR report referred to the excess occurrence of carcinoma of the pharynx in man after therapeutic irradiation of regions of the head and neck.¹ The 1977 Recommendations of the ICRP² do not indicate that the pharynx and hypopharynx would be human tissues at risk in radiation carcinogenesis. However, in a category including all other tissues and organs of the digestive tract, the evidence suggests that in these tissues there is a carcinogenic risk at moderate radiation doses. No experimental radiation carcinogenesis of the pharynx or hypopharynx has thus far been reported in animals. This is of particular interest, in view of the extensive studies on thyroid neoplasia in mice^{1,la} and rats.

Radiotherapy Patients

Cancer of the pharynx and hypopharynx in man has been observed after therapeutic irradiation for benign or malignant conditions in adjacent tissues--frequently the esophagus, the larynx, the thyroid, and the spine.³ Goolden reviewed a series of 37 patients who had previously received radiotherapy for thyrotoxicosis or other lesions of the neck; the latent periods were extremely long (mean, 23.8 yr), the radiation doses were high, and exposure was continuous or fractionated (external radiotherapy fractionated doses of some 3,000-6,000 rads delivered over 3-6 weeks).⁴ Raven and Levinson have reported 10 patients with cancer of the pharynx after radiotherapy; the mean latent period

was 25.0 yr, and doses were in the therapeutic range. Yoshizawa⁵ and Takeuchi reviewed 130 cases of pharynx and larynx radiation neoplasia; the mean latency period was 27.3 yr. Other reports of similar radiation cancers^{6,7} indicate quite long latent periods, in the range of 23-24 yr.

In their study of 14,554 males treated with x-ray therapy⁸ for ankylosing spondylitis, Court-Brown and Doll demonstrated an excess of solid cancers, including cancer of the pharynx, in heavily irradiated sites.⁹ Two groups of patients have been reviewed, each with excess cancers that occurred at least 6 yr after therapy. In the group with complete followup to January 1, 1960 (14,796 man yr), there were four observed cancers of the pharynx and 0.70 expected, for an excess of 3.3 (0.7-8.5).^{*} In the incompletely followed group to January 1, 1963 (165,631 man-yr), the values were five observed and 1.05 expected, for an excess of 3.95 (0.9-9.5; $p > 0.025$; induction rate of 0.300.5^{8,9} per 1,000 patients). However, the number of excess cases of cancer of the larynx over expected was not statistically significant (two cases observed, two expected, and 0.2 excess cases¹⁰ observed over expected). In the most recent followup of the ankylosing-spondylitis patients treated with one course of radiotherapy,¹¹ no significant increase in deaths from cancer of the pharynx over that previously observed was recorded. The ankylosing-spondylitis surveys still require precise dose

*Numbers in parentheses are 90% confidence limits.

estimates for radiation risk to be determined. Risk estimates may be obtainable from this population when radiation dose absorbed by the tissues of the pharynx during radiotherapy has been reliably determined. A mean radiation dose to the spinal canal of 880 rads was estimated for the thoracic spine. However, the induction rate is probably not significantly greater than that observed in the atomic-bomb life span study--perhaps 5-10 excess cases per 10⁶ exposed patients per rad over almost 20 yr of followup.

¹² Radford et al. reported in their survey of mortality among patients with ankylosing spondylitis who were not given x-ray therapy that the only deaths from cancer showing an apparent excess risk were from cancer of the pharynx and hypopharynx (two deaths observed, 0.13 expected, $p < 0.01$). The authors concluded, however, that the numbers were too small to permit firm conclusions concerning a relationship between ankylosing spondylitis and cancer of the pharynx.

Atomic-Bomb Survivors

The Japanese atomic-bomb life span study does not specify pharynx and hypopharynx neoplasia observed in excess, but this may be included in a category of cancer of other digestive organs.

Conclusions

It is important to recognize that the latent period for cancers of the pharynx and larynx is unusually long; mean latent periods exceeding 25 yr have been recorded in some

clinical studies. It follows, therefore, that the values observed in both the atomic-bomb life span study and the ankylosing-spondylitis patients would be below the true values. With a mean latent period of 25 yr, the total number of cancers occurring after irradiation, provided that patients do not die from other causes, would be perhaps only half the number of all cancers induced by radiation. Thus, in the absence of more precise figures of occurrence of cancers and absorbed radiation dose in the pharynx and larynx, only the following limited conclusions can be drawn: there is now a significantly increased rate of induction of cancers of the pharynx in irradiated populations; the mean latent period probably is some 25 yr after exposure; the present value is an underestimate, and a large proportion of radiation cancers of the pharynx and larynx may be expected to occur in surviving populations over the next decade; and any radiation-risk estimates are not precise, because of underestimated values and lack of information on absorbed radiation dose.

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