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EDITORIAL

How Safe for the Patient Is Iodine-131 Therapy for Differentiated Thyroid Carcinoma?

Radioactive ^{131}I has been used in the treatment of well-differentiated thyroid carcinoma over the past fifty years with general agreement from published reports of the safety and efficacy of this treatment, although considerable difference of opinion exists regarding the methodology employed and appropriate restrictions necessary to ensure safety for the patient and others involved (*1*). In the early years of its employment, wide variations in dose from very low to very high provided the experience upon which, in more recent years, dose ranges have been narrowed and techniques have been employed to optimize results.

Because well-differentiated thyroid carcinoma is not uncommon in children and young women in childbearing years, the possibility that this treatment may affect fertility has generated discussion, and these effects have been the subject of several reports (*2,3*). In general, there has been no observable effect based on studies of offspring, although at least one report of ovarian dysfunction after ^{131}I treatment in humans was described (*4*).

Carcinogenesis is also an issue in younger patients. In the early years when larger doses were employed, Brincher et al. described an increase of leukemia in ^{131}I-treated carcinoma patients in Denmark (*5*). However, Hall et al. in Sweden more recently concluded that "no specific cancer or groups of cancers could be convincingly linked to high-dose ^{131}I exposures . . ." (*6*), and that "excess leukemia risks of more than 25% could thus be excluded with high reassurance in this population of mainly adults" (*7*). However, conflicting data have come from Edmonds and Smith in England who found "a small, significant excess of deaths from cancer of the bladder and from leukemia . . ." (*8*). Because most case series are small, it has been difficult to establish the statistical validity of these observations.

With this background, we have in this issue of the *Journal* a paper on the subject of long-term hazards of ^{131}I therapy. Dottorini et al. review the outcome of women with carcinoma of the thyroid treated with ^{131}I to deter-

Received Sept. 12, 1994; accepted Sept. 13, 1994.

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mine the incidence of second neoplasms, female fertility and genetic effects finding elevated incidence of salivary gland tumors and melanoma but no significant differences in fertility rate, birth weight and prematurity (*9*). The addition of this data to the literature of ^{131}I therapy hazards is welcome.

As for carcinogenesis, it is reassuring that no instances of leukemia were observed in the experience reported and the increased incidence of salivary gland tumors is small. The occurrence of melanoma is a little surprising, although melanoma has been reported as a second primary in Edmonds' series (*8*). The data with regard to fertility and genetic effect also confirms what has been previously reported and reinforces that current ^{131}I treatment practices do not jeopardize the fertility potential of the patients treated.

Given the public fear of radiation and the current concept that human exposure to radiation may have been delivered without sufficient caution in past years, we have cause to be extremely careful in weighing the risks and benefits of radiation treatment and to explain these risks to our patients so that they can undergo treatment with knowledge of both benefits and risks. The report offered by Dottorini et al. is a welcome addition to the factual basis upon which this therapy's safety and efficacy rests. It is important to emphasize that ^{131}I remains a very effective therapy for patients with ^{131}I concentrating metastases. Therefore, patients with metastatic disease should not be discouraged from receiving ^{131}I as a treatment modality.

An article by Pacini et al. concerning testicular function in men as determined by serum FSH and testosterone levels before and after therapeutic doses of ^{131}I for differentiated thyroid carcinoma was published recently in the *Journal* (*10*). This study demonstrated progressive increases in FSH level without significant change in testosterone after ^{131}I therapy. There seems little doubt from these data that there is a dose-related effect of ^{131}I on germinal cell dysfunction. It remains unclear whether testicular dysfunction is (a) temporary or permanent (b) related to repeated gonadal exposure or to total dose and (c) clinically correlated with long-lasting infertility. However, this report emphasizes the caution that should be exercised in the size of single and total doses and the necessity to counsel and test wisely when indicated.

One of the uncertainties that will be encountered in counseling patients is the variability in dosimetry which can result based on extent of disease and location and various controllable and uncontrollable aspects of iodine metabolism. The suggestion that ^{131}I doses should be based upon in vivo dosimetry has some appeal in this regard, although methodology has varied between the assessment of only bone marrow dose to the assessment tumor dose (*11*). With this report, it might now be considered that gonadal dose be an important variable which demands attention (*12*). All of this becomes more important as unsealed source therapy expands through the use of labeled monoclonal antibodies and other labeled compounds which will be employed in the future.

In conclusion, therapeutic nuclear medicine is effective treatment for differentiated thyroid cancer with a substantial safety record and continues to provide hope that radioarmaceuticals will play an important role in therapy in the future. However, exposure of normal tissues is a universal characteristic of this form of treatment and effects on radiation-sensitive tissues can be expected. Patients may opt to choose this form of treatment in spite of the risks. For women undergoing treatment with conservative dosimetry, there should be no need to fear infertility or genetic damage. However, because of potential carcinogenesis, doses should be kept within reasonable, accepted limits.

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