INVITED COMMENTARY

^{131}I Therapy: Inpatient or Outpatient?

A widely accepted therapy is ^{131}I for patients with hyperthyroidism caused by Graves' disease, toxic nodular disease, euthyroid multinodular goiters, and differentiated thyroid carcinomas (*1–6*). It has been proven to be a safe and a relatively inexpensive treatment modality. ^{131}I can lead to complete remission, even in thyroid cancer patients with metastatic disease. Therapeutic doses of ^{131}I commonly range from 100 to 7400 MBq, with the larger activities used to ablate thyroid remnants or to treat metastatic disease in patients with thyroid cancer. After a therapeutic administration of ^{131}I, the patient becomes a potential radiation hazard to other individuals. Radiation is emitted from radioactivity in the patient, and radioiodine is secreted in body fluids such as sweat and saliva and excreted into urine and feces. Precautions should be taken to limit the radiation exposure of the nuclear medicine physician, nursing personnel, the patient's family, and members of the public with whom a treated patient may come in contact. These precautions vary between countries, but recommendations are usually based on measurement of ^{131}I retention or instantaneous dose rates. Most patients who receive high doses of ^{131}I are isolated in a private room. The patient is monitored daily, and radiation safety precautions are updated as needed. Nursing care and visitors are limited to nonpregnant adults as necessary. The patients are advised against bringing anything with them that they would be unwilling to leave behind should contamination occur. The patient's radiation exposure is commonly monitored using direct external exposure rate measurements. Alternatively, using fractionated treatment regimens, outpatient treatment schedules have been proposed for large multinodular goiters that commonly require the administration of high doses of ^{131}I (*7*).

In Europe, the administered doses of ^{131}I on an outpatient basis differ among European countries. In Germany, the patient is required to have $<$75 MBq on discharge, which is a rather stringent criteria, giving rise to ^{131}I tourism to neighboring countries, where criteria for release are less stringent. In the United Kingdom, France, Belgium, and The Netherlands, the maximum permissible radioactivity for ambulatory treatment with radioiodine is between 370 and 740 MBq (*8*). Generally, the amount of radioiodine to be administered has been used as the criterion in determination of the need for hospitalization. This is inaccurate on an individual basis because all ^{131}I-treated patients do not necessarily have the same iodine kinetics. For example, public safety may be better preserved if some patients with toxic goiter who are being treated with 400 MBq ^{131}I are hospitalized for longer than some thyroidectomized thyroid cancer patients who receive a much higher ablative dose of ^{131}I because of the rapid clearance of ^{131}I in these thyroid cancer patients. The exposure dose that is considered acceptable for the safety of the general public, resulting from a patient's treatment, has been reduced in Europe after revised recommendations from the International Commission on Radiological Protection (ICRP). The annual public dose limit is 1 mSv, although adult members of the patient's family are allowed to receive higher doses, provided that the average over 5 consecutive years does not exceed 1 mSv/y (*9*).

Barrington et al. (*10*) recently reported that if hyperthyroid patients who were being treated with ^{131}I (dosage range, 195–800 MBq) on an outpatient basis were given appropriate radiation protection advice, they complied with a 5-mSv dose limit (range, 0.2–5.8 mSv) for adults in 97% of cases and with a 1-mSv dose limit (range, 0.2–7.2 mSv) for children in 89% of cases. However, 6 of 17 children, $\leq$3 y old, had a dose that exceeded 1 mSv because they were likely to spend more time in close contact with their mothers than was recommended. In the case of parents of children who are $\geq$3 y old, the preference is not to treat them as outpatients unless arrangements can made for an alternative caregiver for the child after treatment. Furthermore, outpatients treated with 200, 400, 600, or 800 MBq ^{131}I should be advised to sleep alone for 1, 5, 9, or 12 d, respectively (to comply with a 3-mSv dose constraint), and to avoid contact closer than 1 m with children 3–5 y old for 11, 16, 20, or 22 d or with children $>$5 y old for 5, 11, 14 or 16 d to comply with a 1-mSv limit. These constraints are suggested in a recent European Commission guidance document in which dose constraints are linked to age (*11*). On the basis of the recommendations for discharge of patients made by the European Commission, the following dose constraints have been proposed for family and close friends: children (including the unborn child), 1 mSv; adults up to 60 y old, 3 mSv; adults $>$60 y old, 15 mSv; and third persons or general public, 0.3 mSv. In another study, Barrington et al. (*12*) reported radiation dose rates from patients receiving ^{131}I therapy for thyroid cancer. For a patient who received an ablative dose of 1850 MBq ^{131}I, the cumulative dose to nursing staff for a week after treatment depended on patient mobility and was estimated at 0.08 mSv for a self-caring patient to 6.3 mSv for a totally helpless patient. In the follow-up group (residual or recurrent disease), the cumulative doses were

Received Feb. 28, 2000; revision accepted Mar. 28, 2000.

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0.18–12.3 mSv (3700 MBq ^{131}I) or 0.36–24.6 mSv (7400 MBq ^{131}I). If no restriction is applied, cumulative annual doses as high as 103 mSv for the partner and as high as 132 mSv for children <2 y old (administered dose of 7400 MBq ^{131}I in ablation patients) may be obtained. To restrict the dose to 1 mSv, they calculated that partners are required to sleep apart for 3 d (1850 MBq in follow-up of patient) to 23 d in the case of an ablative dose of 7400 MBq. Time restriction of contact with children ranged from 2 to 24 d depending on the dosage and the age of the child.

In the United States, the Nuclear Regulatory Commission (NRC) is charged with protection of health and safety from various radioactive materials, including ^{131}I. The NCR decreased occupational and public radiation dose limits in 1994 from a maximum of 120 mSv/y and an average annual dose of 50 mSv/y to a maximum of 50 mSv in any single year. The radiation dose limit to members of the public, not including patients who received diagnostic or therapeutic radiopharmaceuticals, was reduced from 5 to 1 mSv. For many years the NCR has controlled this potential by requiring medical licensees to hospitalize patients whose administered activity is ≥1100 MBq (30 mCi). As an alternative to this 1100-MBq rule, the hospital is allowed to release the patient when the dose rate is <50 μSv/h at a distance of 1 m from the patient (*13*).

In January 1997, the NCR amended its regulations concerning the criteria for release of patients treated with radiopharmaceuticals (*14*): ''The new criteria for patient release are based on the potential dose to other individuals exposed to the patient. The new criteria are consistent with the recommendations of the National Council on Radiation Protection and Measurements (NCRP) and the International Commission on Radiological Protection (ICRP). This final rule requires the licensee to provide written instructions to patients on how to maintain the dose to others as low as is reasonably achievable, if the total effective dose equivalent to any other individual exposed to the released patient is likely to exceed 1 mSv.'' Furthermore, the NCR proposed a new Code of Federal Regulations, title 10, part 35.75, to change the patient release criteria to a total effective dose equivalent not to exceed 5 mSv in any year to an individual from exposure to a released patient. These proposed changes were supported by the recommendations of the ICRP and NCRP that an individual could be allowed to receive an annual dose up to 5 mSv in temporary situations when exposure to radiation is not expected to result in annual doses >1 mSv for long periods of time (*14*). This dose-based limit also provides a single limit that could be used to provide an equivalent level of risks from all radionuclides. Different radionuclides with the same activity can give very different doses under identical exposure conditions.

The article by Coover et al. (*15*) in this issue of *The Journal of Nuclear Medicine* presents practical data for the treatment of ^{131}I-treated patients as outpatients, in compliance with the Code of the Federal Regulations, title 10, part 35.75. In accordance with these regulations, Coover et al. developed a model to calculate the maximum dose of ^{131}I that may be administered to an outpatient.

An important item in these calculations is the so-called occupancy factor, which consists of 3 separate factors for each of the 3 periods after ^{131}I treatment: the pre-equilibrium period (first 8 h), the constrained activity period (interval after the pre-equilibrium period during which the patient's social interactions are constrained, and the nonconstrained activity period (the following infinite period of time).

Coover et al. (*15*) clearly illustrate the article by examples and tables, which simplify the application of the proposed model. For hyperthyroid patients, the administered dose of ^{131}I will usually be low enough to administer as outpatient treatment. In cases of (toxic) multinodular goiters and in thyroid cancer patients, the formulas and tables described by the authors can be used to establish a maximum dosage. The clinical situation, however, should indicate whether a patient requires a higher dosage, necessitating hospitalization. For example, in thyroid cancer patients with a large metastatic load, the ^{131}I uptake may be much higher than 5% and these patients usually need high doses of ^{131}I (≥7400 MBq).

Application of calculations by Coover et al. (*15*) will enhance patient convenience and facilitate more cost-effective outpatient management. As mentioned by Mountford and O'Doherty (*16*), hospitalizing a patient requires the allocation of expensive resources, and the instructions for a patient after leaving the hospital could cause serious disruption of their domestic and working life. Therefore, hospitalization time and instructions to be followed after discharge should be based on a sound radioprotective assessment and should not be excessively restrictive. The occupancy factors may be based on the patient's lifestyle, including the patient's unique living situation, and on their ability to adopt a set of social limitations for several days.

In addition to the emitted radiation hazard, a contamination hazard from ^{131}I excretion through perspiration, saliva, breath, feces, and urine may arise. This may be as high as 10% of the radiation dose caused by external radiation. This internal radiation exposure resulting from incorporation of ^{131}I should also be considered. Ibis et al. (*17*) reported a relative high skin concentration and specific activity in the saliva of thyroid cancer patients at time of discharge, thus emphasizing the need for instructing patients to prevent significant transfer of ^{131}I to family members and others after release from the hospital.

The use of calculations by Coover et al. (*15*) enables the nuclear medicine physician to determine the maximum ^{131}I dose that can be prescribed for each individual patient. This has many advantages because some patients will choose to sleep apart from their partners for days to weeks, whereas other patients (patients with young children) prefer a short stay in a nuclear medi-

cine ward. Coover et al. note that the use of their model in clinical practice does not preclude alternative release criteria but is predicted on the basis of the new NCR regulations, which are applicable only in NCR states. Nevertheless, the article by Coover et al. contains interesting data for countries other than the United States that are attempting to treat patients with higher ^{131}I doses as ambulatory patients.

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