Treatment of Thyroid Carcinoma: Emphasis on High-Dose ^{131}I Outpatient Therapy

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There is an abundance of evidence indicating that the oral administration of sodium ^{131}I-iodide is of value in the management of well-differentiated thyroid cancers. The first step in the management of thyroid cancer is near-total removal of the thyroid gland. Destroying any residual functioning thyroid tissue in the neck or metastatic tissue elsewhere in the body using ^{131}I after surgery decreases the risk of recurrence and death from well-differentiated thyroid cancers. The dosage of radioiodine used for this purpose varies among different centers. Until a few years ago, radioiodine therapy using >1.110 GBq (30 mCi) ^{131}I required hospitalization of patients to minimize radiation exposure to others. The U.S. Nuclear Regulatory Commission (USNRC) revised Title 10 of the Code of Federal Regulations (10CFR 35.75) in 1997, allowing the release of patients immediately after ^{131}I therapy if the total effective dose equivalent from the patient to an individual does not exceed 5 mSv (0.5 rem) in any 1 y. With this change, which became effective on May 29, 1997, a patient can be treated with a higher amount of ^{131}I as an outpatient and leave the premises with proper instructions to keep the radiation exposure to other individuals as low as it is reasonably achievable.

The objectives of this article are to (a) briefly review the types of thyroid cancer; (b) provide an overall review of the treatment of thyroid carcinomas, follow-up of these patients, and the prognostic indicators of survival; and (c) explain the radiation safety precautions and the preventive measures that can be taken to minimize the radiation exposure of family members or helpers living with the patient and the general public at large.

Key Words: ^{131}I therapy; radioiodine treatment; thyroid cancer; treatment of thyroid cancer

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Cancer of the thyroid may be classified into 2 varieties: those arising from follicular epithelium and from parafollicular or C cells. The carcinoma arising from epithelium consists of papillary, follicular, and anaplastic cell types. The papillary cancers account for approximately 70% of the thyroid cancers, and the incidence of follicular cancer is about 15%–20%. Anaplastic carcinomas constitute about 5% of the thyroid cancers. The remaining 5%–10% represent medullary carcinomas arising from C cells. The medullary cancers may occur as a sporadic form comprising about 80%, and the remaining occur as a familial form. The familial form can occur as part of multiple endocrine neoplasia (MEN) syndrome type 2A or type 2B or in a non-MEN setting. Medullary cancers often secrete thyrocalcitonin, which is detectable in the circulation and can be used as a tumor marker. Medullary carcinomas are generally not iodine avid, and the mainstay of therapy is surgical excision. Although radioiodine has been used to ablate residual thyroid tissue in patients with persistently elevated thyrocalcitonin after total thyroidectomy, its use in medullary carcinoma is controversial (*1*).

Papillary carcinoma, in general, is a slow-growing neoplasm and may spread through the thyroid capsule to structures around the thyroid, especially the lymph nodes. It frequently occurs in the second and third decades and, to a much lesser degree, later in life (sixth or seventh decades) with a mean age of about 45 y. In the young, papillary carcinomas are usually indolent and local invasion is rare. However, in older individuals they are often more aggressive (*2*). Microscopically, it is possible to classify papillary carcinoma of the thyroid into well-differentiated and poorly differentiated varieties. The overall outcome with the well-differentiated variety of papillary carcinoma is very good, whereas the poorly differentiated variety carries a significantly increased risk of death (*3*,*4*). Follicular carcinomas are encapsulated tumors, and they generally tend to occur in older individuals with a mean age about 55 y. They can be seen in younger individuals in whom they behave like a well-differentiated papillary carcinoma. In older individuals, the follicular carcinomas, in general, behave aggressively with a worse prognosis. Overall, in comparison with papillary carcinomas, follicular carcinomas of the thyroid are more aggressive. They have a greater tendency to spread via the bloodstream and metastasize frequently to lung and bone. A rare subtype of follicular carcinoma, Hürthle cell tumor, tends to be more aggressive, with early distant metastases. In the mixed papillary–follicular variety, the follicular elements can be seen to behave aggressively with early distant metastases that are iodide avid (*3,4*).

RADIOIODINE THERAPY

The physician–patient professional relationship implies that the patient consents to the recommendation of the physician with respect to suggested treatment involving radioactivity and absorbed dose. The physician, in fact, has considerable latitude in the ultimate control of the patient's dose. This is based on the accepted principle underlying all administration of radioactive material to a patient. As with any treatment, the benefit derived from the procedure must outweigh the risks associated with the radiation exposure. Although, there are no regulations that limit the dosage administered or the absorbed dose given to a patient, the physician operates under guidelines for appropriate indications for the amount of activity administered, within the bounds of his or her license to use radioactive materials in patients. The U.S. Nuclear Regulatory Commission (USNRC) revised Title 10 of the Code of Federal Regulations (10CFR 35.75) in 1997, so that treatment of patients with a higher amount of radioiodine as an outpatient has become more frequent. However, treating an outpatient with a high dose of ^{131}I poses unique problems, unlike releasing a patient when the total-body retention of ^{131}I is $<$1.110 GBq (30 mCi) (*5*).

GENERAL PRINCIPLE BEHIND ABLATIVE THERAPY AND TREATMENT OF METASTASES USING ^{131}I

Although most thyroid carcinomas can be removed surgically, this involves extensive, methodic, and painstaking surgical procedures to preserve the recurrent laryngeal nerve and the parathyroid glands, which may be embedded in the thyroid gland. The consequence of an aggressive surgical approach produces significant morbidity, sometimes permanent hypoparathyroidism or recurrent laryngeal nerve paralysis. For this reason, a near-total thyroidectomy is the current standard of care. Any residual thyroid tissue may very well be normal tissue without any evidence of malignancy. To localize the possible presence of regional or distant functioning thyroid metastases by radioiodine, however, it is almost always necessary to render any remaining thyroid tissue nonfunctional. The postsurgical residual functioning thyroid tissue can be ablated using ^{131}I. The first report of radioiodine therapy for metastatic thyroid carcinoma was in 1945 (*6*). The efficacy of radioiodine therapy is directly related to tumor uptake and retention. Effective tumor uptake is achieved if there is a concentration of 0.5% of the dose per gram of tumor tissue with an effective half-life of at least 4 d. The radiation absorbed dose delivered to thyroid tissue is related to the activity administered and the fraction of the dose that is taken up by the thyroid tissue. In the above-mentioned situation, administration of 5.55 GBq (150 mCi) ^{131}I would deliver a tumor dose of approximately 25,000 rad (*7*).

The use of radioiodine for treatment of hyperthyroidism, thyroid remnant ablation, or thyroid metastases is based on the radiation-induced cell damage caused by the high-energy β-radiation emitted. ^{131}I is a β-emitting radionuclide with a maximum energy of 0.61 MeV and an average energy of 0.192 MeV (range in tissue, 0.8 mm) and has a principal γ-ray of 364 keV. The magnitude of follicular cell functional damage and reproduction appears directly proportional to the absorbed dose (*8*). Only well-differentiated thyroid cancer cells concentrate radioiodine to a significant degree. These include papillary, follicular, and mixed papillary–follicular cancers. Anaplastic thyroid cancers rarely, if ever, concentrate radioiodine. Medullary thyroid cancers are not generally considered suitable for radioiodine therapy because they do not organify iodine even though they do trap iodine (*9*). As stated earlier, the use of radioiodine treatment in medullary carcinoma is controversial (*1*).

The term "ablation" is generally used to describe destruction of residual functioning thyroid tissue in the neck. Ablation after initial surgery decreases the risk of recurrence and death from well-differentiated thyroid cancers (*10,11*). Radioiodine ablation in a patient with thyroid cancer induces hypothyroidism with resultant elevation of thyroid-stimulating hormone (TSH), which, in turn, stimulates the well-differentiated thyroid cancer cells to concentrate radioiodine. Ablation has been achieved with one or more doses of 925–1,110 MBq (25–30 mCi) ^{131}I (*12,13*). Because hospitalization was not required for patients given $<$1.110 GBq (30 mCi) ^{131}I before the change in 10CFR 35.75, low-dose therapy ($<$30 mCi) was performed in low-risk patients when the patient's convenience superseded other factors. High-dose ablation, however, is recommended for all patients who are at an increased risk of death from well-differentiated thyroid carcinoma—namely, age $>$45 y; poorly differentiated cell type; primary tumor $>$1.5 cm in size; invasion of vessel, lymphatic, or capsule; multifocal cancer; or when there is evidence of metastasis (*11*). 10CFR 35.75 allows outpatient treatment with doses of $>$33 mCi.

PATIENT PREPARATION FOR THERAPY WITH SODIUM ^{131}I-IODIDE

To maximize the radioiodine uptake by residual thyroid tissue or thyroid metastases, pretreatment imaging and treatment are performed when the TSH level in serum is $>$30 μIU/dL. After near-total thyroidectomy, a waiting period of 6 wk is recommended before obtaining a diagnostic total-body ^{131}I scan. At the time of referral to the nuclear medicine physician, if the patient is on triiodothyronine or thyroxine replacement therapy, the thyroid hormone should be discontinued for 2 or 6 wk, respectively, to allow an adequate rise in the TSH level. In the appropriate situation, synthetic TSH produced by recombinant DNA technology may be used to increase the TSH level at the discretion of the physician. Some centers also use a low-iodine diet for 2 wk before diagnostic scanning or ^{131}I therapy to help increase the iodine uptake by functioning thyroid tissue or metastases. Medication containing iodine, and medications that can alter iodine uptake and utilization, should be avoided before treatment for an appropriate duration of weeks or months depending on their effect on iodine metabolism (e.g., amiodarone, kelp, radiographic contrast agents, cough syrups, and so forth). Written informed consent may be obtained as stipulated by the local or state rules and regulations.

When it comes to unnecessary radiation, it is always better to be prudent and extra conservative; hence, we recommend that female patients of childbearing age should be instructed not to become pregnant in the first year of treatment and they should be screened for pregnancy before giving the ^{131}I dose. In addition, it is the responsibility of the nuclear medicine physician to make them fully aware of the possible need for additional ^{131}I treatment. Once the follow-up ^{131}I diagnostic study is considered normal, female patients can be told that they may conceive. If the patient becomes pregnant within the first year of treatment, this will preclude further treatment, if needed, until the baby is born. Because iodine is secreted in the breast milk, ^{131}I should not be given to nursing mothers unless alterative feeding and nourishment of the infant can be accomplished and prolonged close contact with the mother can be avoided. Once the patient elects alternative feeding of her infant, then appropriate medications can be given for cessation of lactation to prevent unnecessary radiation absorbed dose to the lactating breasts. All of the circumstances and concerns mentioned above can be avoided with proper education of female patients about radiation and its effects on the fetus, infants, and the mammary glands before treatment.

A total-body radioiodine scan after thyroidectomy is obtained to evaluate the presence and extent of residual functioning thyroid tissue in the neck and its radioiodine uptake value. This information is necessary to estimate the dose of ^{131}I required for therapy. The total-body scan may also reveal unsuspected metastatic foci in the neck or elsewhere. It is important to note that the dose of ^{131}I administered for the diagnostic scan can exert a negative effect by reducing the uptake of the ensuing therapeutic dose by the residual functioning thyroid tissue in the neck or any metastatic tumor; this phenomenon is referred to as "thyroid stunning" (*14,15*). The degree of thyroid stunning is considered to be directly proportional to the diagnostic dose used (*15*). Although debates continue as to the practical significance of stunning, it has become a common practice to use only 74 MBq (2 mCi) to 111 MBq (3 mCi) sodium ^{131}I-iodide for preablation or pretreatment diagnostic scans.

Most nuclear physicians prefer fixed-dose ^{131}I therapy without actually calculating the dosimetry for ablation. The treatment dose variances among various centers are wide, with a range of 1.85 GBq (50 mCi) to 7.4 GBq (200 mCi), depending on whether it is given for residual functioning thyroid tissue in the neck or for metastases detected locally in the neck or in various organs and the age and sex of the patients. First doses as high as 11.1 GBq (300 mCi) have been given in some centers on the basis of the assumption that the metastases may subsequently lose their ability to concentrate iodine (*16*).

The following dosage schedule has been proven to be effective and practical for (a) functioning tissue in the thyroid bed, 3.7 GBq (100 mCi); (b) cervical node metastases, 5.55 GBq (150 mCi) to 6.475 GBq (175 mCi); (c) lung metastases, 6.475 GBq (175 mCi) to 7.4 GBq (200 mCi); and (d) skeletal metastases, 7.4 GBq (200 mCi) (*17*). As noted earlier, ablation of the residual functioning thyroid tissue has been achieved with 1 or more doses of 925–1,110 MBq (25–30 mCi) ^{131}I. This may be performed in low-risk patients when the patient's convenience and reduction in cost are a consideration (*12,13*).

When using high-dose therapy, the dose to the blood should be <200 rad to reduce bone marrow toxicity. The total whole-body retained dose at 48 h should be <4.44 GBq (120 mCi) in widespread metastatic thyroid carcinoma and 2.96 GBq (80 mCi) when there are lung metastases (*16,18*). The latter is a precaution to avoid inducing pulmonary fibrosis.

SELECTION AND MANAGEMENT OF OUTPATIENTS RECEIVING HIGH-DOSE ^{131}I

Once the clinical parameters indicate the need for high-dose outpatient radioiodine therapy, additional patient assessment is necessary in reference to patient selection. Patients should be mentally alert and physically able to take care of themselves without much assistance from family members or friends. Patients should be able to walk to the bathroom without difficulty and be able to use the toilet as necessary without urine contamination outside the toilet. Both oral and written patient instructions for limiting radiation exposure to family members and others are of utmost importance. This should be done systematically and care should be taken that the patient and any family members residing with or planning to help the patient understand all of the instructions (Table 1). If there is concern that the patient is unreliable or incapable of following the instructions, and there are no close family members or friends who would be responsible for ensuring that the patient follows all of the instructions, then it is advisable to treat the patient as an inpatient. If liquid ^{131}I is to be used for therapy, appropriate use of a closed-circuit liquid radioiodine delivery system may limit or eliminate, even in the absence of a fume hood, contamination of the ambient air and skin and the possibility of any accidental spillage.

Consideration must be given to prevent exposure to the general public and family members. The USNRC regulations (*5*) stipulate that a total effective dose equivalent should not exceed 5 mSv (0.5 rem) in any 1 y to an individual from exposure to a released patient after ^{131}I

TABLE 1
Instructions

Patient instructions	Duration (d)		
	1.11–3.7 GBq* (30–100 mCi)	3.7–5.55 GBq* (100–150 mCi)	5.55–7.4 GBq* (150–200 mCi)
To reduce external exposure to others			
Limit time spent in public places	2	3	4
Limit private travel (at 0.914-m separation of >2 h)	1	2	3
Do not travel by mass transportation or airplane	2	3	4
Do not travel on prolonged automobile trip with others	2	3	4
Delay returning to work if workplace or office is shared	2	3	4
Avoid prolonged close contact with children and pregnant women	4	5	6
Sleep in separate bed (>1.829-m separation)	4	5	6
Flush used facial tissues down the toilet (flush toilet, at least twice, after urination)	4	5	6
To minimize transfer of ^{131}I or internal exposure			
Avoid mouth-to-mouth contact	4	5	6
Do not share items that contact mouth or saliva (e.g., eating utensils, water/pop/beer bottles/cans, etc.)	4	5	6
Use separate towels and washcloths	4	5	6
Use regular utensils and plates and wash them separately	4	5	6
Wash your hands thoroughly after going to toilet (use separate bathroom, if possible, and men should also sit down while urinating)	3	4	5

*Treatment dose range.

Based on NRC Regulatory Guide 8.39 and James E. Carey, Jr., MS, DABR presentations at Society of Nuclear Medicine meetings and local presentation in December 1998.

therapy. Transportation home after ^{131}I therapy needs to be planned. If patients are fit enough to drive home alone, then transportation is not an issue. In fact, most patients cannot drive properly because of their hypothyroid status or their general medical condition after major thyroid surgery. A significant number of the patients who have been off thyroid hormone replacement after thyroidectomy complain that they are tired and unable to stay awake when they report for the diagnostic total-body ^{131}I scan. The radioiodine treatment is usually given, if needed, 1 or more days after the scan is obtained, depending on the convenience of the patients, their family members or their helpers, and the availability of the radiopharmaceutical. In the days after the scan, the patient's hypothyroid symptoms may worsen. In this situation, we believe it is not wise to advise the patients to drive home by themselves after treatment. Transportation to the patient's residence after treatment should be, preferably, in a private automobile or a taxicab. The larger the vehicle, the better, unless the duration of travel is limited (Table 1) to avoid exposure to other individuals. As a conservative estimate, an individual driving a patient who has received 200 mCi ^{131}I in a medium-sized automobile, with an estimated distance between the patient and the driver of 0.5 m and for a duration of 30 min, will receive a dose of approximately 88 mrem (*19*). If the patient chooses public transportation, a distance between the patient and other passengers of 0.5 m or more may not always be achieved, and there may be children or pregnant women in close proximity. We recommend that children should not accompany patients during their return travel home after treatment even for a short distance because the accepted dose limit for a minor is one tenth that of an adult.

If children must reside in the patient's residence, a private bedroom and bath for use by the patient is recommended. If the home is small and crowded, such that there are no facilities to limit the absorbed dose to <5 mSv (500 mrem) in a year to an adult family member living with the patient, then the patient should be treated with high-dose ^{131}I as an inpatient. The patients should be instructed to limit the time spent in public places the first few days and avoid places such as theaters, sport arenas or stadiums, and so forth, where the option of getting a seat farther away from others may not always be possible.

In the first 24 h, radioiodine therapy patients excrete between 30% and 75% of the administered dose. Most of it is in the urine but a significant amount enters the gastrointestinal tract via salivary excretion and gastric secretion. Measurable amounts are also secreted in perspiration. Although details of radiation containment and reduction of personal exposure have been discussed regarding inpatient treatment with ^{131}I (*20*), a few points need to be stressed when treating patients with high-dose ^{131}I as an outpatient. It is important that patients are instructed to be careful not to spill any urine and to flush the toilet 2 or 3 times after use. If the toilet area is carpeted, we suggest diaper pads or diaper sheets be used to cover the carpet using tape so that any accidental spillage of urine on the carpet can be prevented. We advise men to urinate while sitting on the toilet to prevent possible contamination outside the toilet. At our institution we recommend that any contaminated flushable part of the diaper pads should be flushed down the toilet and the remainder washed in a tub using gloved hands before discarding into the trash. We recommend that female patients with urinary incontinence limited to only minor dribbling use a half-inch (1.27 cm) stack of facial tissues, as needed, and the soiled stack of tissues should be flushed down the toilet. The thickness of a tissue stack can be increased to an inch (2.54 cm) or so depending on the degree of incontinence and the patient's convenience. All of the commercially available products for urinary incontinence have some part or component that does not flush down the toilet and must be discarded in the trash. If any of these products are used, then the nonflushable nylon or plastic component needs to be washed in a tub before discarding into the trash. If the underwear gets soiled, it should be washed in a tub by the patient or her helper with gloved hands. These recommendations will vary to some degree from institution to institution. Male patients with urinary incontinence should be advised to use a condom catheter with a urine collection bag, which should be emptied as frequently as practicable. The condom-catheter-bag set should be thoroughly soaked in ammonia-containing detergent for several minutes and rinsed using gloved hands before discarding in the household trash. Patients and the helper should be advised to wash their hands thoroughly after any cleaning of contaminated items. The bathroom sink and tub should be thoroughly rinsed after each use.

During the first week of therapy, patients should be advised to wear only machine-washable clothing because a measurable amount of radioactivity is secreted in perspiration and the soiled clothes should be washed separately. If a patient has been caring for an infant before treatment, she or he should be specifically instructed to avoid any close contact with the infant for several days after treatment. If there is need for contact, then the utmost care should be taken to keep contact and the time spent to a minimum. If there are other members in the household, continuous close contact or proximity should be avoided. Any time spent with an individual should be short, and a distance of >1 m should be maintained (Table 1).

Measurable amounts of radioiodine are excreted in the feces. In fact, on total-body scans, a relatively intense radioiodine distribution is generally seen throughout the large colon on the second and the third days, more so on the third day. Therefore, a laxative, taken on the second or at least the third night, will stimulate faster elimination of radioiodine-containing feces and reduce the radiation absorbed dose to the abdominal organs, the thoracolumbosacral spine, and the pelvis. To keep the radiation exposure "as low as it is reasonably achievable" is considered a good practice by the authors. During the first weeks of therapy, if it is necessary for patients treated with ^{131}I to seek other medical evaluation or treatment for any reason, the patients should be instructed to inform the medical personnel of the radioiodine treatment they have received.

Because a significant amount of dose is excreted in the saliva, any facial tissues that are used in the first few days should be flushed down the toilet and should not be disposed of in normal trash. The patients should be specifically instructed to avoid foods that would potentially get contaminated with saliva while eating and have residue that needs discarding (e.g., chicken wings, ribs, fruits with a core, and so forth). Fruits, such as apples, can be consumed after cutting into pieces and discarding the core. Fruits with a core can be disposed of into the public sewage by the use of a garbage disposal. Deboned chicken can be eaten without concern of contaminating the household trash. Foods such as chicken wings eaten in the first few days after treatment with ^{131}I can result in bones contaminated with radioiodine from the patient's saliva. Discarding them in the trash that is picked up by a public garbage truck may result in the truck being impounded at the entrance to a landfill depending on how stringent the local regulations are (*21*).

To avoid contaminated disposable utensils going into the normal trash, it is advisable and recommended to exclusively use personal plates, glassware, and silverware. These are to be cleaned by the patient (or a helper with gloved hands) in a private bathroom sink and kept in the patient's room for daily use for 1 wk. Alternatively, a dishwasher can safely be used to clean the plates and utensils without cross-contamination.

A patient's failure to observe the instructions resulted in an accident in the authors' local community. In this incident, a garbage truck was stopped at the entrance to a landfill because of a significant radiation level detected with a survey meter. The truck was impounded and prohibited from dumping its contents and was left in a corner of the landfill site over the weekend. The initial few days of the incident were very difficult for the local residents, mayor, and the local radiation safety officers. When the survey was repeated on Monday (3 d after the original reading) and significant radioactivity was again detected, the state department of environmental conservation got involved. A survey of all of the houses on the route from which the particular truck picked up garbage localized a house with radioactive garbage. Further investigation indicated that the resident of the house had received ^{131}I 2 d before the garbage truck picked up the trash. The reason for the presence of radioactivity in the garbage was due to facial tissues from a patient. The patient had received a 3.7-GBq (100 mCi) dose of ^{131}I and was suffering from a cold and cough. A similar situation due to a low-level threshold setting of the survey meter at the landfill site resulted in the impounding of another truck (*21*,*22*).

SIDE EFFECTS OR COMPLICATIONS OF ^{131}I THERAPY FOR THYROID CARCINOMA

Significant side effects are rare with doses around 3.7 GBq (100 mCi). However, dose-related sialadenitis, nausea, vomiting, gastritis, loss of taste, radiation cystitis, conjunctivitis, keratoconjunctivitis, and other side effects, including decreased testicular function, have been reported (*23–25*). The use of lemon drops in the first few days may help decrease the incidence and severity of radiation sialadenitis and absorbed radiation dose to the salivary glands. An extremely minimal increased risk of leukemia and bladder, breast, and salivary carcinomas has been noticed when the cumulative dosage exceeds $>$37 GBq (1.0 Ci) in $<$1 y (*18*,*23*,*25*,*26*).

FOLLOW-UP OF PATIENTS AFTER ^{131}I THERAPY

Patients are given replacement thyroid hormones beginning on the third day of therapy at a low-dosage level, especially if they have cardiac problems. The authors prefer the administration of a small dose (25 μg) of triiodothyronine daily along with thyroxine in noncardiac patients during the first week because of its rapid pharmacologic action with prompt improvement in patients' hypothyroid symptoms. The thyroxine dose has to be adequate to suppress the TSH to a normal range (we prefer the middle to low-normal range), and the level should be monitored every 4 wk until a definitive maintenance dose is found.

Obtaining a scan (ablative or treatment) after therapy is a good way of assessing the presence and the extent of metastases, and additional findings or more accurate localization of metastases has been reported in 46% cases (*27*). The scan after therapy is usually obtained 5–8 d after treatment, depending on the treatment dose used. If no radioiodine uptake was documented other than insignificant (0.5%) residual functioning thyroid tissue in the thyroid bed, then only the patients who show an elevation of thyroglobulin levels are rescanned at 6 mo; otherwise, the follow-up scan is deferred for a year in the authors' practice. However, the follow-up protocols differ widely among different centers. Elevation of the serum thyroglobulin level signals the presence of metastatic disease in patients on replacement thyroid therapy; therefore, routine thyroglobulin levels are obtained every 3–6 mo. A diagnostic total-body ^{131}I scan is obtained, as and when necessary, after discontinuing thyroid hormone replacement therapy or after the administration of synthetic TSH (as mentioned under patient preparation for therapy). Even if the scan is negative for metastases in the presence of an elevated serum thyroglobulin level, ^{131}I treatment has shown reduction in thyroglobulin levels, indirectly demonstrating a therapeutic effect (*28*,*29*).

PROGNOSTIC FACTORS OF SURVIVAL

On review of the findings published from the 1960s through the 1980s, age was found to be a major prognostic factor. Survival was found to be better when the age was $<$40 y. In a review of 70 fatal cases of papillary thyroid carcinoma, the average age of members of the fatal group at the time of initial treatment was 52 y, whereas that of the surviving group was 39 y (*30*). Large-sized tumors, extrathyroid spread, and anaplastic changes were present in a significant proportion of fatal cases. In the experience of Halnan (*31*), a constant inverse correlation was found between the age at diagnosis and survival in 344 unselected patients with thyroid cancer. Mazzaferri et al. (*32*) found a higher proportion of recurrence in patients under the age of 30 y but a significantly greater proportion of mortality in those over the age of 40 y. Despite more incidences of recurrence in large symptomatic primary cancers, survival was not adversely affected. Deaths were more common in those patients who had tumors $>$2.5 cm in diameter. No statistical differences were found between those who had lymph node metastases and those who did not. Further, no difference in survival could be documented between patients who had undergone lymph node dissection and those who had not.

Risk definition based on the age, presence of distant metastases, extent of primary tumor, and size of the tumor was done by Cady and Rossi (*33*). According to their findings, the high-risk group included all patients with distant metastases, all older patients with extrathyroidal papillary cancer or major capsular involvement with follicular cancer, and all primary cancers $>$5 cm in size regardless of the extent of disease. The low-risk group included all young patients, men $<$41 y and women $<$51 y, without distant metastases; all older patients with intrathyroidal papillary cancer; and primary cancers $<$5 cm in diameter without any metastases. On a 20-y follow-up, the low-risk group of 277 patients (89%) had only 5% recurrences and 1.8% death. During the same period of time, the high-risk group of 33 patients (11%) had 18 recurrences (55%) and 15 deaths (45%).

The European Organization for Research on Treatment of Cancer–Thyroid Cancer Cooperative Group proposed a prognostic index based on age, sex, cell type, clinical activity of tumor, lymph node status, and number of metastatic sites in 500 patients with thyroid carcinoma (*34*). They used survival from all causes of death as the endpoint and established a total score based on multiple prognostic factors. There was a direct correlation between an increased scoring index and the death rate from cancer. Tennvall et al. (*35*) reconfirmed that age at diagnosis, extent of local tumor, and distant metastases are important prognostic factors.

As stated above, the age is an important factor, with a cutoff at 40 y for males and 50 y for the females: The younger age groups fare better than the older ones. The follicular cancers have a tendency to metastasize to distant sites, whereas lymph node metastases are common with papillary thyroid cancers (*36*). The most common sites for distant metastatic disease are lungs (45%), bone (29%), both (10%), and other sites, including liver, brain, and kidney (*37*). Papillary carcinoma of the thyroid is much less aggressive than the follicular type. The overall 10-y survival after initial therapy of papillary thyroid carcinomas was found to range from 87% to 92%, whereas follicular carcinomas showed a range of 43%–94% depending on patient selection (*38*).

CONCLUSION

In the overall management of patients with differentiated thyroid carcinomas, a program consisting of a near-total thyroidectomy, high-dose ablative therapy for aggressive cell type or patients with metastases, adequate TSH suppressive therapy, periodic assessment of the serum thyroglobulin level, appropriate use of ^{131}I whole-body scanning, and repeated ^{131}I therapy as needed can reduce the recurrence rate and increase survival. The radiation safety precautions that should be used must be discussed with both the patient and the family members to minimize radiation exposure to the family and to the general public. With proper education and instructions to the patients and their family members, the radiation exposure to themselves and the general public can easily be minimized.

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REFERENCES

1. Saad MF, Ordonez NG, Rashid RK, et al. Medullary carcinoma of the thyroid: a study of the clinical features and prognostic factors in 161 patients. *Medicine.* 1984;63:319–342.
2. McConahey WM, Taylor WF, Gorman CA, et al. Retrospctive study of 820 patients treated for papillary carcinoma of the thyroid at Mayo Clinic between 1946 and 1971. In: Andreoli M, Monaco F, Robbins J, eds. *Advances in Thyroid Neoplasia*. Rome, Italy: Field Educational Italia; 1981:245–262.
3. Tscholl-Ducommun J, Hedinger CE. Papillary thyroid carcinomas: morphology and prognosis. *Virchows Arch [A]*. 1982;396:19–39.
4. Sakamoto A, Kasai N, Sugano H. Poorly differentiated carcinoma of the thyroid: a clinicopathologic entity for a high-risk group of papillary and follicular carcinomas. *Cancer.* 1983;52:1849–1855.
5. Tuttle WK 3rd, Brown PH. Applying nuclear regulatory commission guidelines to the release of patients treated with sodium iodine-131. *J Nucl Med Technol.* 2000;28:275–279.
6. Seilini SM, Marinelli LD. Therapeutic effect of radioactive iodine on adenocarcinoma of the thyroid with functioning metastases [abstract]. *Bull NY Acad Med*. 1945;21:440.
7. Maxon HR, Thomas SR, Hertzberg VS, et al. Relation between effective radiation dose and outcome of radioiodine therapy for thyroid cancer. *N Engl J Med.* 1983;309:937–942.
8. Malone JF. The radiation biology of the thyroid. *Curr Top Radiat Res Q.* 1975;10:263–368.
9. Parthasarathy KL, Shimaoka K, Bakshi SP, et al. Radiotracer uptake in medullary carcinoma of the thyroid. *Clin Nucl Med.* 1980;5:45–48.
10. Varma VM, Beirwaltes WH, Nofal MM, et al. Treatment of thyroid cancer: death rates after surgery and after surgery followed by sodium iodide-I131. *JAMA.* 1970;214:1437–1442.
11. Hurley JR, Becker DV. Treatment of thyroid carcinoma with radioiodine. In: Gottschalk A, Hoffer PB, Potchen EJ, Berger HJ, eds. *Diagnostic Nuclear Medicine*. Vol 2. Edition 2. Baltimore, MD: Williams & Wilkins; 1988.
12. McCowen KD, Adler RA, Ghaed N, et al. Low dose radioiodide thyroid ablation in postsurgical patients with thyroid cancer. *Am J Med.* 1976;61: 52–58.
13. Leung SF, Law MW, Ho SK. Efficacy of low-dose iodine-131 ablation of post-operative thyroid remnants: a study of 69 cases. *Br J Radiol.* 1992; 65:905–909.
14. Jeevanram RK, Shah DH, Sharma SM, et al. Influence of initial large dose on subsequent uptake of therapeutic radioiodine in thyroid cancer patients. *Nucl Med Biol.* 1986;13:277–282.
15. Muratet JP, Daver A, Minier JF, et al. Influence of scanning doses of iodine-131 on subsequent first ablative treatment outcome in patients operated on for differentiated thyroid carcinoma. *J Nucl Med.* 1998;39:1546–1550.
16. Leeper RD. Controversies in the treatment of thyroid cancer: the New York Memorial Hospital approach. *Thyroid Today.* 1982;5:1–4.
17. Beierwaltes WH. Radioiodine therapy of thyroid disease. *Nucl Med Biol.* 1987;14:177–181.
18. Bushnell DL, Boles MA, Kaufman GE, et al. Complications, sequela and dosimetry of iodine-131 therapy for thyroid carcinoma. *J Nucl Med.* 1992; 33:2214–2221.
19. Vilani J. How to determine the appropriateness of release for a radioiodine therapy outpatient. Presented at: The 47th Annual Meeting of the Society of Nuclear Medicine; June 5, 2000; St. Louis, MO.
20. Thompson MA. Radiation safety precautions in the management of the hospitalized 131-I therapy patient. *J Nucl Med Technol.* 2001;29:61–66.
21. Culver CM, Dworkin HJ, Forsaith A. Disposal of small quantities of radioactive materials in local landfills: problem and solutions. *J Nucl Med.* 1993;34:349–350.
22. Wilkerson A, Klein RC, Party E, et al. Low-level radioactive waste from U.S. biomedical and academic institutions: policies, strategies and solutions. *Annu Rev Public Health*. 1989;10:299–317.
23. Alexander C, Bader JB, Schaefer A, et al. Intermediate and long-term side effects of high-dose radioiodine therapy for thyroid carcinoma. *J Nucl Med.* 1998;39:1551–1554.
24. Solans R, Bosch JA, Galofre P, et al. Salivary and lacrimal gland dysfunction (sicca syndrome) after radioiodine therapy. *J Nucl Med.* 2001;42:738–743.
25. Van Nostrand D, Neutze J, Atkins F. Side effects of “rational dose” iodine-131 therapy for metastatic well-differentiated thyroid carcinoma. *J Nucl Med.* 1986;27:1519–1527.
26. Dottorini ME, Lomuscio G, Mazzucchelli L, et al. Assessment of female fertility and carcinogenesis after iodine-131 therapy for differentiated thyroid carcinoma. *J Nucl Med.* 1995;36:21–27.
27. Spies WG, Wojtowicz CH, Spies SM, et al. Value of post-therapy whole-body I-131 imaging in the evaluation of patients with thyroid carcinoma having undergone high-dose I-131 therapy. *Clin Nucl Med.* 1989;14:793–800.
28. Ruiz-Garcia J, Ruiz de Almodovar JM, Olea N, et al. Thyroglobulin level as a predictive factor of tumoral recurrence in differentiated thyroid cancer. *J Nucl Med.* 1991;32:395–398.
29. Pacini F, Lippi F, Formica N, et al. Therapeutic doses of iodine-131 reveal undiagnosed metastases in thyroid cancer patients with detectable serum thyroglobulin levels. *J Nucl Med.* 1987;28:1888–1891.
30. Tollefsen HR, De Cosse JJ, Hutter RVP. Papillary carcinoma of the thyroid: a clinical and pathological study of 70 fatal cases. *Cancer.* 1964;17:1035–1044.
31. Halnan KE. Influence of age and sex on incidence and prognosis of thyroid cancer: three hundred forty-four cases followed for ten years. *Cancer.* 1966;19:1534–1536.
32. Mazzaferri EL, Young RL, Oertel JE, et al. Papillary thyroid carcinoma: the impact of therapy in 576 patients. *Medicine.* 1977;56:171–196.
33. Cady B, Rossi R. An expanded view of risk-group definition in differentiated thyroid carcinoma. *Surgery.* 1988;104:947–953.
34. Byar DP, Green SB, Dor P, et al. A prognostic index for thyroid carcinoma: a study of the E.O.R.T.C. Thyroid Cancer Cooperative Group. *Eur J Cancer.* 1979;15:1033–1041.
35. Tennvall J, Biorklund A, Moller T, et al. Is the EORTC prognostic index of thyroid cancer valid in differentiated thyroid carcinoma? retrospective multivariate analysis of differentiated thyroid carcinoma with long follow-up. *Cancer.* 1986;57:1405–1414.
36. Simpson WJ, McKinney SE, Carruthers JS, et al. Papillary and follicular thyroid cancer: prognostic factors in 1578 patients. *Am J Med.* 1987;83: 479–488.
37. Norton JA, Levin B, Jensen RT. Cancer of the endocrine system. In: DeVita VT Jr, Hellman S, Rosenberg SA, eds. *Cancer, Principles and Practice of Oncology.* Vol 2. Edition 4, Philadelphia, PA: J.B. Lippincott; 1993:1333–1435.
38. Frazell EL, Foote FW Jr. Papillary cancer of the thyroid: a review of 25 years of experience. *Cancer.* 1958;11:895–922.

CONTINUING EDUCATION TEST: Treatment of Thyroid Carcinoma: Emphasis on High-Dose ^{131}I Outpatient Therapy

For each of the following questions, select the best answer. Then circle the number on the CE Tests Answer Sheet that corresponds to the answer you have selected. Complete the answer sheet. Keep a record of your responses so that you can compare them with the correct answers, which will be published in the next issue of *JNMT* after the test return deadline. Answers to these test questions should be returned on the Answer Sheet no later than **December 31, 2003.** An 80% correct response rate is required to receive 1.0 CEH (Continuing Education Hour) credit for each article. SNM Technologist Section members can find their VOICE number on the upper left-hand corner of their *JNMT* mailing labels. If you've joined our Nonmember VOICE Tracking Program, please write *NMVTP* on the Answer Sheet (no extra fee is required). Documentation will appear on your VOICE transcript. Nonmembers who have not joined our Nonmember VOICE Tracking Program must mail a $10.00 check or money order, made payable to SNM, for each completed quiz. You will receive a certificate of completion indicating credit awarded for receiving a passing score of 80% or better. All articles are approved by the Florida Department of Health Bureau of Radiation Control.

A. *What is the main consideration for the release of patients administered high-dose ^{131}I?*

101. The proximity of the patient's home to the hospital.
102. Radiation exposure of the public and family members.
103. Radiation sickness effects that the patient may experience.
104. ^{131}I released into the local sewer system from the patient's home.

B. *Which types of thyroid carcinomas are most iodine avid and best suited to ^{131}I therapy?*

105. Anaplastic thyroid cancers.
106. Medullary thyroid cancers.
107. Poorly differentiated anaplastic and medullary thyroid cancers.
108. Well-differentiated thyroid cancers: papillary and follicular.

C. *The term "ablation" refers to:*

109. Radiation therapy of distant thyroid metastases.
110. Destruction of functioning thyroid tissue in the thyroid bed (in the neck).
111. The suppression of TSH.
112. All of the above.

D. *Which patients are candidates for high-dose ($\geq$1,221 MBq [$\geq$33 mCi]) ^{131}I therapy?*

113. Hyperthyroid patients.
114. Patients with iodine-avid thyroid metastases.
115. Patients who are at high risk with anaplastic thyroid carcinoma.
116. 113 and 115.

E. *Which statement is true:*

117. Ablation can be accomplished with a low dose (<1,110 MBq [<30 mCi]) in selected situations of papillary thyroid carcinoma.
118. Ablation can be successfully accomplished after a thyroidectomy regardless of the TSH level in the blood.
119. A preablation or pretreatment diagnostic scan is best accomplished with a high dose (296–370 MBq [8–10 mCi]) of ^{131}I.
120. Thyroid "stunning" is not seen with high doses of ^{131}I.

F. *Which of the following statements regarding the management of urinary incontinence is true?*

121. Tissue can be used to absorb minor leakage and then flushed down toilet.
122. Toilets should be flushed twice after each use.
123. Male patients can use a condom-type catheter with urine bag.
124. All of the above.

G. *Which of the following practices will help avoid contamination of garbage that will be picked up by local trash collection contractors?*

125. Staying home from work 5–7 d after therapy.
126. Flushing tissues down the toilet.
127. Using paper plates, cups, and plastic utensils.
128. All of the above.

H. *Which of the following is the least important prognostic factor for thyroid carcinoma?*

129. Age.
130. Distant metastases.
131. Sex.
132. Size.
133. Cell type.

I. *Which of the following practices will help to minimize radiation exposure to others?*

134. Avoid close contact with children and pregnant women for 4–6 d.
135. Avoid public places and transportation where the patient is likely to have close contact with others for 2–9 d.
136. Sleep in a separate bed for 4–6 d.
137. All of the above.

J. *Which of the following statements regarding patient preparation for ^{131}I therapy associated with thyroid cancer is correct?*

138. There is no patient preparation for this ^{131}I therapy.
139. The patient must have a bowel-cleansing preparation (enemas and laxatives) before starting the whole- body scan and therapy dose.
140. The patient's serum TSH level should be >30 μIU/dL.
141. Female patients of childbearing age should not become pregnant within the first 2 mo after ^{131}I therapy.

K. *Which of the following statements regarding treatment of women of childbearing age is correct?*

142. Women of childbearing age with thyroid cancer should not be treated with ^{131}I.
143. Female patients of childbearing age should have a pregnancy test before ^{131}I therapy.
144. Female patients of childbearing age who have been treated with ^{131}I may become pregnant after a 1-y follow-up ^{131}I diagnostic study is considered normal.
145. Female patients of childbearing age should not become pregnant within the first 2 mo after ^{131}I therapy.
146. 143 and 144.

L. *^{131}I therapy patients should not be released after therapy if the exposure to other individuals is likely to exceed:*

147. 5 mSv (0.5 rem) in any 1 y.
148. 0.5 mrem/h the first 48 h after therapy.
149. 10 mrem.
150. All of the above.

Answers to CE Article Test #1, Sep 2001

The CE article "Maintaining a Proper Perspective of Risk Associated with Radiation Exposure" by Thompson was accompanied by a CE test. The correct answers are:

A. 102	D. 113	G. 126	J. 134	M. 146
B. 106	E. 118	H. 128	K. 140	N. 152
C. 112	F. 121	I. 130	L. 142	O. 155

Answers to CE Article Test #2, Sep 2001

The CE article "Epidemiology for the Nuclear Medicine Technologist" by Bolus was accompanied by a CE test. The correct answers are:

P. 158	S. 171	V. 183	Y. 196
Q. 164	T. 176	W. 186	Z. 200
R. 165	U. 178	X. 189	

Note: Answers to the CE tests in this issue will be given in the March 2004 issue.

CONTINUING EDUCATION TEST #1
Interpretation and Reporting of Myocardial Perfusion SPECT

Answer Sheet

101	104	107	110	113	116	119	121	123	125	127	129	131	133	135
102	105	108	111	114	117	120	122	124	126	128	130	132	134	136
103	106	109	112	115	118									

Name ______________________ Title ______________________

Hospital or Facility ______________________ Dept. ______________________

Street Address ______________________

City ______________________ State ______ Zip ________ Phone (____) ______________

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Today's Date ______________________ Florida JX number ______________________

Return a copy of this answer sheet no later than **December 31, 2003,** to:
Jannine Jordan, Continuing Education Coordinator, *Journal of Nuclear Medicine Technology,* the Society of Nuclear Medicine, 1850 Samuel Morse Dr., Reston, VA 20190.
FAX: 703-708-9015.

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Remember, you can also take these exams on the SNM Web site, at www.snm.org!

CONTINUING EDUCATION TEST #2
Treatment of Thyroid Carcinoma: Emphasis on High-Dose ^{131}I Outpatient Therapy

Answer Sheet

101	104	107	110	112	114	116	118	120	122	124	126	128	130	132
102	105	108	111	113	115	117	119	121	123	125	127	129	131	133
103	106	109												

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