Side Effects of "Rational Dose" Iodine-131 Therapy for Metastatic Well-Differentiated Thyroid Carcinoma

Douglas Van Nostrand, Janet Neutze, and Francis Atkins

Nuclear Medicine Service, Uniformed Services University of Health Sciences, Walter Reed Army Medical, Washington, DC

Benua, Leeper, and others (BEL) have advocated the estimation of radiation exposure to the blood to select a more rational maximum safe dose of radioiodine (dosimetry) to treat metastatic functioning well-differentiated thyroid carcinoma. After adopting the BEL dosimetry approach, we reviewed the immediate (during hospitalization) and intermediate (from discharge up to 3 mo) side effects after our initial 15 therapies in ten patients. The doses ranged from 51 mCi (1,887 MBq) to 450 mCi (16.65 GBq). Immediate side effects were observed in 12/15 (80%), are described in detail, and were as follows: gastrointestinal 10/15, salivary 9/15, nonsalivary neck pain, swelling, etc. 2/15, pulmonary 0/15. Intermediate side effects were observed in 10/15 (67%), are described in detail, and were as follows: gastrointestinal 0/15, salivary 3/15, nonsalivary neck pain, swelling, etc. 3/15, nasal complaints 2/15, transient bone marrow suppression 9/10, pulmonary 0/15. No patient required blood transfusions or had complications secondary to reduced blood counts. All patient complaints resolved; however, several patients may have reduced baseline blood counts one year after therapy. No other long-term side effect has been noted but the mean follow-up has been only 15 mo. In our opinion, we have not observed any side effect to date which would contraindicate the continued use and evaluation of the BEL dosimetry approach.

J Nucl Med 27:1519–1527, 1986

Radioactive iodine is widely used in the treatment of metastatic well-differentiated functioning thyroid carcinoma; however, the dose is controversial and usually arbitrary (i.e., up to 200 mCi, 7.4 GBq) (*1–3*). Benua, Leeper, and others (BEL)* have advocated a more rational approach to dose selection based upon dosimetric studies to estimate maximum safe exposures to the blood (dosimetry) (*2,4*). The BEL dosimetry not only identifies patients who might have significant side effects from a standard, arbitrary dose such as 200 mCi (7.4 GBq), but it also allows patients to be treated with doses as high as 600 mCi (22.2 GBq) with acceptable side effects to date. Benua and Leeper have followed this approach for over 20 years and Leeper reviewed their experience in 1973 and 1980 (*5,6*). However, to our knowledge no other institution has reported their experience using this approach. In September 1982 the Walter Reed Army Medical Center instituted this approach, and the purpose of this report is (a) to review our preliminary experience of immediate (during hospitalization) and intermediate (after discharge up to 3 mo) side effects resulting from iodine-131 (^{131}I) treatments based on doses calculated by the BEL dosimetric approach, and (b) to describe these side effects in more detail than previously reported.

Received Oct. 28, 1985; revision accepted Mar. 7, 1986.

For reprints contact: Douglas Van Nostrand, MD, HSHL-XN, Nuclear Medicine Service, Walter Reed Army Medical Center, Washington, D.C. 20307-5001.

PATIENTS AND METHODS

Patient Eligibility for Dosimetry

Eligibility was determined by histologically proven well-differentiated (papillary/follicular) thyroid carcinoma and distant metastasis defined as soft-tissue invasion (e.g., esophageal), mediastinal lymph node, bone, lung, liver, and/or brain (cervical node metastasis without soft-tissue invasion were not included).

Patient Eligibility for ^{131}I Therapy Based on Dosimetry

Eligibility was determined by (a) a scan demonstrating functioning metastasis; (b) thyroid stimulating hor-

mone (TSH) >40 uU; (c) "low" likelihood of pregnancy (i.e., premenarchal, postmenopausal, within 7 days of menses, history of abstinence, and/or negative beta-HCG, etc.); (d) agreement by patient to practice birth control for at least 1 yr; and (e) informed consent.

Patient Preparation

Thyroxine was discontinued 6 wk prior to dosimetry, and triiodothyronine (typically 25 μg p.o. t.i.d.) was begun 6 wk prior to dosimetry and discontinued 3 wk prior to dosimetry. A low iodine diet was initiated 3 wk prior to dosimetry and discontinued upon release from therapy isolation room. The typical daily fluid intake was maintained. On the initial day of dosimetry, T4, RT3U, $RIAT_3$ TSH, thyroglobulin, and complete blood count (CBC) with differential were obtained.

Technical Aspects of Dosimetry Protocol

Data collection. The technical aspects of the BEL dosimetry protocol have been previously described (*2, 4,5*) and will be summarized here. At standard time intervals following the oral administration of a 5 mCi (185 MBq) dose of ^{131}I (reduced in children), blood specimens, urine collections, and whole-body counts are obtained. The blood specimens and whole-body counts are routinely obtained 0, 2 (whole body only), 4, 24, 48, 72, and 96 hr after dosing. All urine is collected separately for each 24-hr period for 4 days. This is the minimum observation period. If the whole-body retention has not fallen below ~2% of the administered dose, then these measurements are continued at 24-hr intervals until either (a) the whole-body retention is ≤2% or (b) the clearance is determined to be approximately the physical half-life. The whole-body counts are obtained for 2-min intervals using a single 5 × 5 in. NaI(Tl) detector at a distance of 14 ft. Linearity quality control of the detector was performed to assure that no dead-time corrections were necessary for the dose of ^{131}I used. The geometric mean of the background corrected anterior and posterior counts is used as the estimate of whole-body activity. These data are then be used in calculating the biological uptake and clearance of oral iodine by the individual patient.

Whole-body imaging. Seventy-two hours after the administration of the tracer dose of ^{131}I, images are obtained of the head, proximal upper and lower extremities, anterior and posterior chest, and posterior abdomen using a gamma camera† equipped with a general purpose iodine collimator‡. Images are obtained for 20,000 counts or 45 min, whichever occurs first. Additional images and/or delayed images are obtained at the discretion of the clinic physician.

Calculation of maximal safe dose. The calculation of the maximal safe dose has been previously described (*2,4,5*). Areas enclosed in brackets represent modification to Benua's original approach. "Briefly, the beta radiation dose to the blood is calculated by integrating the area under the blood curve formed by the daily blood measurements over approximately [5 days]. In this manner, after using suitable decay factors the average beta dose to blood per mCi-day can be calculated. Physical decay only after day [5] is used. Using the factor of 10 rad to a liter of blood per mCi-day the beta dose to blood can be calculated. In the same manner, integrated whole body retention calculated by subtracting percentage of dose excreted/day from 100% is determined, the integrated area under the curve determined, and the gamma contribution to whole-body radiation can be calculated by the formula 20.4 rad/mCi-day/kg × 0.4 where 0.4 is the fraction of gamma radiation affecting blood. Beta and gamma calculations are summed and the predicted radiation dose/mCi of ^{131}I to blood is obtained" These calculations are performed by a computer program. Doses are selected to give a maximum of 200 rad (2Gy) to the blood, with no more than 120 mCi (4.44 GBq) retained in the whole body at 48 hr. In the presence of diffuse lung metastasis, no more than 80 mCi (2.96 GBq) should be retained in the whole body at 48 hr.

Selection of Dose

The final selected dose for administration is based upon the above calculated doses, complete blood count (CBC), and/or response of CBC to any previous therapy. Doses were reduced in arbitrary amount if (a) the baseline WBC count was < 4,000 or (b) the WBC dropped 50% or more of baseline during the 8 wk post-therapy period of the previous treatment. Since we have only been approved for a maximum of 420 mCi (15.54 GBq), no prescribed single dose exceeded this limit.

Therapy

The patient is hospitalized for the therapy and reverse radiation isolation is implemented following treatment. After informed consent, the patient is treated with the selected dose of ^{131}I and is encouraged to drink a typical daily fluid intake. If fluid intake is not maintained, then intravenous fluids would be administered. Patients are encouraged to chew gum, eat sour candies, or drink diluted lemon juice during the first day until bed time to promote discharge of radioiodine from salivary glands.

Patients are discharged after the health physicist confirms that the patient's whole-body retention of ^{131}I is below the regulatory limits.

Documentation of Side Effects

A retrospective review was performed on four patients by reviewing inpatient, outpatient, thyroid and nuclear medicine charts, and by interviewing all patients. The remaining patients were prospectively evaluated during the hospital admission with follow-up interviews with patient and referring physician. Side effects are reported by both organ system and time of occurence from therapy. The latter were divided into immediate (during hospitalization), intermediate (after discharge up to three mo) and long term (after three mo of treatment). A drop in any blood count (hemo-

globin, white blood cell count or platelet count) of 10% or more of the baseline was considered a side effect.

RESULTS

To date, a total of 12 patients have had 17 dosimetric calculations performed. Two patients had no demonstrable ^{131}I uptake and, consequently, they were not treated. Thus, ten patients had 15 dosimetric calculations which were used to help select the ^{131}I dose for therapy. One patient has received three therapies, and three patients have received two therapies. Table 1 displays the age, site of metastasis, previous total dose of ^{131}I, months since previous therapy, calculated dose by whole-body and blood specimens ("uptake"), calculated dose by urine data and blood specimens ("urine"), administered dose, and side effects. The ages ranged from 6 to 41 yr, and 8 were female; 2 were male. The mean follow-up was 15 mo with a range of 4 to 30 mo. Eight patients had papillary carcinoma, and two patients had follicular carcinoma. The distribution of metastatic sites were as follows: (a) four with mediastinal and/or cervical nodes and all had soft tissue invasion, (b) one with bone metastasis only, (c) two with lung metastasis only, (d) one with cervical node and lung metastasis only, (e) one with cervical, bone, and lung metastasis, and (f) one with either bone and/or lung metastasis (localization of the metastasis could not be accurately determined). The administered dose was approximately equal to the calculated dose (±10%) in seven of the treatments. Eight of the treatments required a reduction in the dose, because (a) four doses would have exceeded our Radiation Control Committee's maximum allowable limit, (b) three patients had a low baseline white blood cell count and/or a previous drop in white blood cell count of over 50%, and (c) one patient would have refused blood transfusions if needed. In the latter four patients, the amount of reduction in dose was arbitrary. No patient was administered a dose greater than the calculated dose.

The dose calculated by the whole-body "uptake" data was with ±10% of the dose calculated by the whole body "urine" data in 11 of 13 therapies. In two therapies the dose calculated by the whole-body "uptake" data exceeded the dose calculated by the whole-body "urine" data by 61% (Patient 3, therapy 2) and 18% (Patient 9 therapy 2). In these two therapies, the urine collection was known to be technically incomplete, which would result in an apparently higher retention of the dose.

Side Effects

Salivary

Symptoms or signs of side effects of the salivary gland occurred in ten of 15 (67%) therapies with pain in six, tenderness in three, swelling in three, and unpleasant (bitter) taste and/or dry mouth in five. These occurred typically on the day after therapy, were mild, and resolved within 2 hr to 3 days. The pain and tenderness were easily controlled with aspirin, except in one case (Patient 6, therapy 2) who had poorly controlled pain, tenderness, and swelling lasting 3 wk. (As discussed below, this may have been secondary to tumor necrosis in part or in toto.) A complaint of dry mouth which persisted for longer than 3 mo was infrequent (1/15), and the complaint of dry mouth subsequently resolved.

Possible Tumor Necrosis

Two patients receiving a total of three therapies complained of diffuse neck pain involving areas, typically not salivary gland. In Patient 6 (therapies 2 and 3) described above, the pain and/or swelling occurred during hospitalization and lasted 3 wk. The pain and swelling in Patient 2 occurred 1 wk after therapy and lasted 2 wk. Both patients had extensive cervical metastasis with soft tissue invasion. In both cases, the pain and/or swelling may have been secondary to tumor necrosis. No other side effects that could be classified as secondary to tumor necrosis were observed.

Gastrointestinal

Gastrointestinal complaints were observed in ten of 15 (67%) therapies. Six patients complained of mild nausea without vomiting and the complaints usually occurred within 36 hr and as early as 2 hr. The nausea typically lasted from 1 hr to 2 days and the nausea either required no treatment or was easily controlled with anti-emetics. Severe nausea without vomiting occurred in one patient (Patient 6, therapy 2) and required intravenous anti-emetics because oral and rectal anti-emetics were ineffective. Nausea with vomiting occurred on the day following treatment in two patients, and one patient described a generalized ill-defined abdominal discomfort which persisted for 2 days. No diarrhea or other symptoms/signs of untoward effects of the gastrointestinal system were noted.

Bone Marrow

None of the patients required a blood transfusion, and of the ten therapies with follow-up CBC data available from their primary physician, nine had a transient drop in one or all values. A typical response is shown in Fig. 1 (Patient 5, therapy 3), and the most severe response is shown in Fig. 2 (Patient 1, therapy 2). A comparison of the baseline (pretherapy) CBC with the CBC approximately 1 yr later is shown in Table 2. Although the number of patients (five patients, six therapies) is too small for statistical evaluation, the data suggest that the baseline WBC may be decreased 1 yr after therapy. In Patient 1, therapy 1, the 10,000 WBC may not have represented a true baseline, since the patient had just recovered from an infection.

Pulmonary

Four patients with pulmonary metastasis have received a total of six treatments, and no acute radiation pneumonitis has been observed. One patient (Patient

TABLE 1
Patient Data

Patient no.	Therapy no.	Age (yr)	Site of metastasis	Previous total dose of ^{131}I (mCi)	Months since previous therapy	Dosimetry Estimates		^{131}I Dosed (mCi)
						Uptake*	Urine*	
1	1	6	Cervical node; diffuse lung; bone	0	N.A.	51	52	51
	2	7	Cervical node; diffuse lung; bone	51	10	97	90	97
	3	8	Lung; (bony uptake resolved)	148	12	241	X‡	185§
2	2	32	Mediastinal; soft tissue invasion of esophagus	200	17	597	584	300¶
3	2	41	Cervical and mediastinal nodes; lung and/or bone (ribs)	143	12	557	347	300**
4	2	33	Cervical nodes; lung	200	10	279	271	275
5	2	40	Bone	195	8	356	335	350
	3	41	Bone	545	12	572	612	410††
6	2	39	Cervical and mediastinal nodes	100	9	358	327	352
	3	40	Cervical and mediastinal nodes	452	11	500	536	350§
7	1	23	Mediastinal nodes	0	N.A.	260	238	230
8	2	21	Cervical nodes; mediastinal nodes; soft tissue invasion with adhesion to esophagus and trachea	150	11	601	X‡	414††
	3	23	Cervical and mediastinal nodes (different pattern)	664	19	538	528	402††
9	2	24	Lung	50	5	663	560	450††,‡‡
10	2	27	Lung	104	30	423	401	400

* See text.
† All times are time from therapy.
‡ X = Not available.
§ Dose reduced because of blood count response to previous therapy.
¶ Dose reduced because patient would refuse blood transfusion.
** Dose reduced because of low baseline WBC.
†† Dose reduced because it exceeded maximum allowable for our institution.
‡‡ Dose administered was 150 mCi followed 6 days later by 300 mCi.

1), who has diffuse miliary pulmonary metastasis, has been treated three times and has no evidence of radiation fibrosis by chest x-ray or pulmonary function tests after 2.5 yr of observation from the first treatment and after 6 mo from last treatment. The other three patients have no evidence of radiation fibrosis, but the follow-up periods have only been 4, 4, and 12 mo, respectively.

Nasal

Two patients had complaints related to the nose. One had a dry nasal mucosa at ~1 wk followed by easily controlled epistaxis. The other patient had a tender nose with clots and "scabs" during the second week post-therapy. Presently, neither has any complaints related to the nose.

Other

Although no patient has developed any serious untoward effects such as leukemia, anaplastic transformation, hypoparathyroidism, or any other head or neck tumors, the follow-up period is too short to make any conclusions. Spermatogenesis was not evaluated.

Temporal Correlation of the Onset of Side Effects to Time of Therapy

The immediate side effects and their frequency are shown in Table 3. Immediate side effects were observed in 12 of 15 (80%) patients and gastrointestinal complaints were the most frequent. The intermediate side effects and their frequency are shown in Table 4. Intermediate side effects were observed in 10 of 15 (67%)

TABLE 1
Patient Data (*continued*)

Side Effects†				
Salivary	Neck area (nonsalivary)	Gastrointestinal	Peripheral blood counts	Other
—	—	—	No data	—
—	—	Nausea on Day 2	Transient drop (see Fig. 2)	—
—	—	—	Transient drop	—
—	Mild neck pain 1–3 wk	Mild nausea at 2–8 hr	No change	—
Mild pain at 24–48 hr	—	Nausea at 4 hr; vomiting at 12–14 hr easily controlled	Transient drop	Dry nasal mucosa with epistaxis at 1 wk; pain in auxillary node
Tenderness on Day 2	—	Nausea on Day 2	Transient drop	—
Mild pain at 24 hr	—	—	Transient drop	—
—	—	Mild abdominal discomfort Days 1–2	Transient drop (see Fig. 1)	—
Swelling pain, tenderness in entire neck region involving salivary & nonsalivary metastatic areas (several days to several weeks)		Nausea at 14–36 hr	Transient drop	—
Bitter taste with loss of other taste for 3 wk				
Swelling in entire neck region but less severe, and no pain or tenderness (several days to several weeks)		Severe nausea at 14 hr controlled with i.v. intravenous antiemetics	Transient drop	
Dry mouth for over 3 mo, since resolved				
Mild pain at 24–28 hr	—	Nausea at 4–6 hr	Data incomplete, no evidence of decreased count	—
Unpleasant taste several weeks after discharge	—	—	No data	
Unpleasant taste; mild pain on Day 2	—	—	Transient drop	—
Pain on Day 2 with mild swelling	—	Vomiting on Day 1	No data	—
Abnormal taste; slightly tender glands on Day 3	—	Mild nausea on Day 1	No data	Tender nose with clots from 1–2 wk

* See text.
† All times are time from therapy.
‡ X = Not available.
§ Dose reduced because of blood count response to previous therapy.
¶ Dose reduced because patient would refuse blood transfusion.
‖ Dose reduced because of low baseline WBC.
†† Dose reduced because it exceeded maximum allowable for our institution.
‡‡ Dose administered was 150 mCi followed 6 days later by 300 mCi.

patients and bone marrow suppression was the most frequent. The long term side effects to date are shown in Table 5. The total number of therapies is too small to demonstrate any relation of the various side effects to either (a) total administered activity, (b) total administered activity per kilogram, (c) individual administered activity, or (d) the ratio of the actual individual administered activity to the calculated activity.

DISCUSSION

The BEL dosimetry approach is based on several rationales. First, one can argue empirically that a universal, single dosage of ^{131}I is not the best therapy for all metastatic carcinoma. Second, conjecturally, the largest dose of ^{131}I that is considered safe and therapeutic should be used because functioning metastases may lose their ability to function and take up ^{131}I yet continue to grow after repeated small doses of irradiation (*7*). Third, the estimation of a therapeutic dose needed to kill a tumor is very difficult if not impossible and it does not address safety (*8*). Fourth, although calculation of exposure to critical organs is also very difficult if not impossible, the side effects of the dose can be observed and used to modify future doses for that patient and/or to modify the dosimetry procedure for other patients. Taken together, these factors comprise the rationale for the BEL dosimetry approach.

We have adopted this approach because of the above rationales and because the approach has been used for

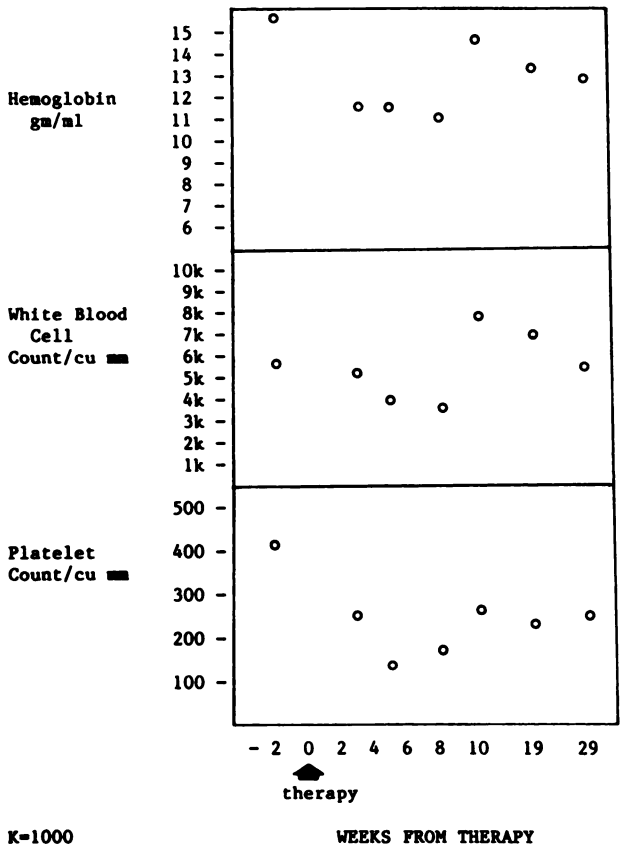

FIGURE 1
(K = 1,000) Typical observed response of hemoglobin levels, white blood cell counts, and platelet counts after therapy with dosages determined with aid of BEL dosimetry (Case 5, therapy 3). (See text)

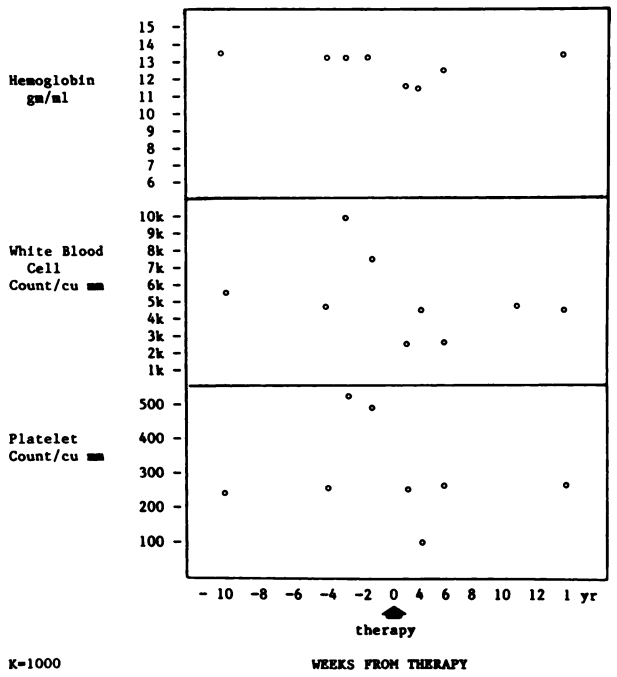

FIGURE 2
(K = 1,000) Most severe observed response of hemoglobin levels, white blood cell counts, and platelet counts after ^{131}I therapy with dosages determined with aid of BEL dosimetry (Case 1, therapy 2). (See text)

~25 years with side effects which are in our opinion acceptable.

In evaluating the BEL dosimetry approach, cost, patient benefit, and side effects must be considered. Financial cost was not evaluated, and although Leeper has reviewed his experience (*5–6*), patient benefit is yet to be established. The purpose of this report was to review the side effects of the BEL dosimetry approach when used in our hands and to describe the side effects in more detail than originally reported by Benua and Leeper (*4–6*).

A comparison of the side effects reported by Benua (*4*), Leeper (*5–6*), and this report are shown in Table 6. The side effects reported by Benua (*4*) were before the implementation of the restrictions as noted at the bottom of Table 6; all other reports were after the implementation of the restrictions. Benua (*4*) also reported one case each of thrombophlebitis of a leg, alopecia over metastasis, and aspermia which were not included on Table 6.

Our frequency of gastrointestinal, salivary, possible tumor necrosis, and bone marrow side effects was higher than that reported initially by Benua. Although we are not certain of the reason for the discordancy, it is possible that it is related to the definition of side effects, the degree of prospective observations, and/or the thoroughness of chart and history review. A general review of side effects of ^{131}I therapy for thyroid carcinoma has been previously published (*1*); however, no data are available to accurately compare frequency and severity of side effects from the standard dose of 200 mCi (7.40 GBq) and the dose calculated by the BEL dosimetric approach.

In summary, an attempt to individualize the dose of ^{131}I is a logical approach and BEL dosimetry is one such approach based upon an estimate of maximum safe exposure to the bone marrow. In our hands, the types of side effects were similar to those reported by Leeper (but this could be due to our bias in reviewing charts and interviewing patients). The frequency of side effects appears to be greater but this may be secondary to a more detailed patient history and review on our part. Nausea, sialoadenitis, and bone marrow suppression were typically observed and vomiting, possible tumor necrosis, epistaxis, and/or xerostomia were infrequently observed. Radiation pneumonitis, pulmonary fibrosis, and new cancers (i.e., leukemia) were not observed; however, the number of patients and mean follow-up are limited. All observed side effects resolved and/or

TABLE 2
Comparison of Pretherapy CBC with CBC 1 year later*

Blood counts	Patient no.	Therapy no.	Pretherapy	Post-therapy	Percent† change
Hemoglobin g/ml	1	1	13.0	13.3	+2
	1	2	13.3	13.5	+2
	4	2	12.5	12.6	+1
	5	2	16.0	15.6	−3
	6	2	12.4	13.5	+9
	8‡	2	16.0	13.3	−17
WBC counts/cu mm					
	1	1	10.0 k	5.3 k	−47
	1	2	5.3 k	4.8 k	−9
	4	2	6.1 k	6.0 k	−2
	5	2	5.3 k	5.6 k	+6
	6	2	5.7 k	4.0 k	−30
	8	2	6.0 k	4.6 k	−23
Platelet counts/cu mm	1	1	307 k	249 k	−19
	1	2	249 k	269 k	+8
	4	2	248 k	266 k	+7
	5	2	236 k	282 k	+19
	6	2	300 k	356 k	+19
	8	2	260 k	227 k	−13

* No intervening therapy.
† + = increase; − = decrease from baseline.
‡ Two years between intervening therapy.

were easily treatable and no blood transfusions or complications of bone marrow suppression have occurred. During hospitalization the side effects were gastrointestinal, salivary, and/or possible tumor necrosis in origin. During the period following discharge from hospital up to 3 mo, side effects were salivary and bone marrow in origin. In our opinion, no side effect has been observed which contraindicates the continued use of BEL dosimetry to aid in the selection of ^{131}I doses. In addition, the BEL dosimetry aided in the selection of pediatric doses and may potentially identify adult patients whose maximum safe dose is less than the frequently used 200 mCi (7.40 GBq).

In regard to BEL dosimetry, further research is clearly needed in (a) determining type and frequency of long term side effects (i.e., xerostomia, leukemia), (b) establishing if there is improved patient morbidity and mortality from thyroid cancer relative to other methods of dose selection, and (c) methods to reduce side effects and/or long term complications such as sialoadenitis and xerostomia. Nevertheless, until this data is available, one must still make a decision based on inadequate information regarding whether or not to treat with ^{131}I and, if ^{131}I is selected, how much ^{131}I should one use. If BEL dosimetry is used we believe the physician should (a) make a firm commitment to the procedure with compulsive collection of data, (b) see a significant number of patients eligible for treatment, (c) perform a good follow-up which allows modification of

TABLE 3
Immediate Side Effects (During Hospitalization)

Side effect	Percent of patients
Any side effect	12/15
Gastrointestinal	10/15
Salivary	9/15
Neck pain (nonsalivary)	2/15
Pulmonary	0/15

TABLE 4
Intermediate Side Effects (After Discharge up to 3 Mo)

Side effect	Percent of patients
Any side effect	10/15
Gastrointestinal	0/15
Salivary	3/15
Neck pain and/or swelling (nonsalivary)	3/15
Nasal complaints	2/15
Bone marrow suppression	9/10
Acute radiation pneumonitis	0/15
Radiation fibrosis	0/15

TABLE 5
Long-Term Side Effects* (Greater than 3 Mo)

Side effect	Number of patients
Salivary (dry mouth)	1
Nonsalivary neck	0
Gastrointestinal	0
Bone marrow	?
Pulmonary	0
Nasal	0
Other	0

*To date.

either future doses for the individual patient or the dosimetric procedure itself, (d) assure that the patient gives an informed consent, and (e) obtain approval by the appropriate regulatory organization.

FOOTNOTES

*Multiple authors including R.S. Benua, R. Leeper, R.W. Rawson, J.E. Rall, and others, have contributed to and deserve recognition for the development of the Memorial Sloan Kettering Cancer Center dosimetry approach. We have arbitrarily chosen the acronym "BEL" (pronounced "bell") to refer to their approach and to simplify communication.

†Picker 415 gamma camera, Picker International, Highland Heights, OH.

‡Picker International, Highland Heights, OH.

ACKNOWLEDGMENTS

The authors thank Ms. Lorraine Woodruff for her secretarial support, without which this manuscript would not have been possible. The authors also thank Robert Leeper, MD, and Leonard Wartofsky, MD, for their suggestions and comments.

TABLE 6
Reported Immediate and Intermediate Side Effects

Side effect	Benua (2*, 4)	Leeper (2, 5)	Present report
Gastrointestinal			
Nausea	44/122†	NR‡	9/15
Vomiting	30/122	NR	2/15
Diarrhea	1/122	~<5%	0/15
Total§	44/122 (36%)	~33%	10/15 (67%)
Salivary			
Unpleasant taste	3/122	NR	5/15
Dry mouth (xerostomia)	3/122	Common	2/15
Sialaodenitis	3/122	NR	9/15
Total	9/122 (7%)	Common	10/15 (67%)
Thyroid metastasis			
Erythema	1/122		
Pain	8/122	NR	2/15
Swelling	0/122 (<1%)	NR	3/15
Total	9/122 (4%)	NR	3/15 (20%)
Bone marrow			
Transient	30/122¶	Frequent	9/10**
Severe suppression	6/122	0/?	0/10
Fatal	2/122	0/?	0/10
Total	38/122 (31%)		9/10 (90%)
Pulmonary			
Pneumonitis	3/59	0/?	0/15
Fatal	2/59	0/?	0/15
Total	5/59 (8%)	0/?	0/15 (0%)

*Prior to implementation of restriction of maximum (a) 200 rad total blood radiation, (b) 120 mCi of ^{131}I whole-body retention at 48 hr, and (c) 80 mCi of ^{131}I whole-body retention at 48 hr if pulmonary metastases are present.

† = Total number of therapies.

‡NR = Not reported.

§ = Number of patients with any sign or symptom.

¶ = Hemoglobin 10 g Hgb/dl or less, WBC <3,000/cu mm, platelets <100,000/cu mm.

** = A drop in any blood count of 10% or more of baseline.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of the Defense.

REFERENCES

1. Freeman LM, Weissmann HS: *Nuclear Medicine Annual 1983*, New York, Raven Press, 1983, pp 329–384
2. Leeper RD, Shimaoka K: Treatment of metastatic thyroid cancer. *Clin Endocrinol Metab* 9:383–404, 1980
3. Beierwaltes WH: Controversies in the treatment of thyroid cancer: The University of Michigan approach. *Thyroid Today* 6:1–5, 1983
4. Benua RS, Cicale NR, Sonenberg M, et al: The relation of radioiodine dosimetry to results and complications in the treatment of metastatic thyroid cancer. *Am J Roent Rad Ther Nuc Med* 87:171–182, 1962
5. Leeper RD: The effect of I-131 therapy on survival of patients with metastatic papillary or follicular thyroid carcinoma. *J Clin Endocrinol Metab* 36:1143–1152, 1973
6. Leeper RD: Controversies in the treatment of thyroid cancer: The New York Memorial Hospital approach. *Thyroid Today* 5:1–4, 1982
7. Rawson RW, Rall JE, Peacock W: Limitations and indication in treatment of cancer of thyroid with radioactive iodine. *J Clin Endocrinol* 11:1128–1142, 1951
8. Maxon HR, Thomas SR, Hertzberg VS, et al: Relationship between effective radiation dose and outcome of radioiodine therapy for thyroid cancer. *N Engl J Med* 309:937–941, 1983