The major etiologic factor for thyroid cancer is childhood or adolescent exposure to head and neck radiation. Previously, radiation was used to treat an enlarged thymus, tonsillar disease, hemangioma, or acne. More recently, exposure to radiation from nuclear plants (e.g., Chernobyl, Ukraine) contributed to an increased incidence of thyroid cancer. Patients with a history of irradiation should have a baseline thyroid ultrasound study, and careful palpation of their thyroid every 1 to 2 years.

A dominant nodule (>1 to 1.5 cm) or nodules with ultrasound features compatible with neoplasia should undergo FNA, which is a safe procedure that has reduced the need for surgical excision. An expert cytologist can identify most benign lesions (75% of all biopsies). In addition, malignant lesions (5% of biopsies), such as papillary, anaplastic, and medullary carcinomas, can be specifically identified. Follicular neoplasms, however, cannot be diagnosed as benign or malignant by FNA; a cytology report of follicular neoplasia, along with "suspicious" cytology, requires surgical excision. Molecular testing can now be performed on FNA specimens to help determine whether follicular lesions have molecular characteristics of malignancy and should be removed. If the patient has a follicular lesion and a suppressed TSH level, a thyroid scan should be performed, because hot nodules are rarely malignant.

Although in the past benign thyroid nodules were treated with levothyroxine suppression, this is no longer recommended because it is uncommon for thyroid nodules to shrink substantially with levothyroxine.

THYROID CARCINOMA

The types and characteristics of thyroid carcinomas are presented in Table 63-7. Papillary carcinoma is associated with local invasion and lymph node spread. Indicators of poor prognosis include thyroid capsule invasion, size greater than 2.5 cm, age at onset older than 45 years, tall cell or Hürthle cell variant, and lymph node involvement. Follicular carcinoma is slightly more aggressive than papillary carcinoma and can spread by local invasion of lymph nodes or hematogenously to bone, brain, or lung. Many tumors show both papillary and follicular cell types. Patients may exhibit metastases before diagnosis of the primary thyroid lesion. Anaplastic carcinoma tends to occur in older individuals, is very aggressive, and rapidly causes pain, dysphagia, and hoarseness.

Medullary thyroid carcinoma is derived from calcitonin-producing parafollicular cells and is more malignant than papillary or follicular carcinoma. It is multifocal and spreads both locally and distally. It may be either sporadic or familial. When familial, it is inherited in an autosomal dominant pattern and is part of multiple endocrine neoplasia type IIA (medullary carcinoma of the thyroid, pheochromocytoma, and hyperparathyroidism) or multiple endocrine neoplasia type IIB (medullary carcinoma of the thyroid, mucosal neuromas, intestinal ganglioneuromas, marfanoid habitus, and pheochromocytoma). Elevated basal serum calcitonin levels confirm the diagnosis. Evaluation for *RET* proto-oncogene mutations should be performed in patients with medullary carcinoma; if mutations are present, all first-degree relatives should be examined.

Treatment

Lobectomy may be performed for isolated papillary microcarcinoma. However, larger papillary tumors and most follicular tumors require thyroidectomy with a central compartment lymph node dissection, as well as a modified neck dissection if evidence of lateral lymph node metastases is found. After surgery, patients with low-risk, small carcinomas may be administered doses of levothyroxine sufficient to keep the TSH level in the low-normal or slightly suppressed range and monitored with serum thyroglobulin determinations and neck ultrasound examinations. Patients with large lesions and those at high risk for persistence or metastatic disease should be treated with radioactive iodine. Sufficient levothyroxine is then administered to suppress serum TSH to subnormal levels. Frequent clinical and ultrasound neck examinations for masses should be accompanied by measurement of serum thyroglobulin levels.

Thyroid cancer patients are considered to have no residual disease if neck ultrasound imaging studies are negative and serum thyroglobulin is suppressed after recombinant TSH stimulation. Recurrence and metastases are also evaluated by ^{131}I whole body scans carried out under conditions of TSH stimulation, which increase ^{131}I uptake by the thyroid tissue. Elevated TSH levels can be achieved by withdrawal of thyroxine supplementation for 6 weeks or by treatment with recombinant human TSH administered while the patient maintains therapy with thyroid hormone replacement. The latter avoids symptomatic hypothyroidism. A rise in serum thyroglobulin levels suggests recurrence of thyroid cancer. Local or metastatic lesions that take up ^{131}I on whole body scanning can be treated with radioactive iodine after the patient has stopped thyroid hormone replacement, whereas those that do not take up ^{131}I can be treated with surgical excision or local x-ray therapy. Conventional chemotherapy has limited efficacy in the treatment of differentiated thyroid cancer, but newer biologic agents targeting the molecular pathogenesis of these tumors appear promising.

TABLE 63-7 CHARACTERISTICS OF THYROID CANCERS

TYPE OF CANCER	PERCENTAGE OF THYROID CANCERS	AGE AT ONSET (YR)	TREATMENT	PROGNOSIS
Papillary	80	40-80	Thyroidectomy, followed by radioactive iodine ablation	Good
Follicular	15	45-80	Thyroidectomy, followed by radioactive iodine ablation	Fair to good
Medullary	3	20-50	Thyroidectomy and central compartment lymph node dissection	Fair
Anaplastic	1	50-80	Isthmusectomy followed by palliative x-ray treatment	Poor
Lymphoma	1	25-70	X-ray therapy or chemotherapy or both	Fair