



# Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology

**MEDICAL MANAGEMENT UPDATE** Editors: F. John Firriolo, Craig S. Miller, and Nelson I. Rhodus

## Thyroid disorders. Part III: neoplastic thyroid disease

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This paper is part III of the series on thyroid disorders. Thyroid tumors are the most common endocrine neoplasms. Most of these tumors are benign hyperplastic or colloid nodules or benign follicular adenomas. However, 5% to 10% of the lesions that come to medical attention are carcinomas. A major clinical challenge is establishing which nodules are hyperplastic, benign, or malignant. History, clinical findings, ultrasonography, and fine-needle aspiration biopsy are the mainstays for diagnosis. There are 3 main histologic types of thyroid cancer: differentiated, medullary, and anaplastic. Differentiated lesions are subdivided into papillary, follicular, and Hurthle cell carcinomas. In addition, primary lymphoma may occur in the thyroid gland and other cancers may metastasize to the thyroid. An important neoplastic syndrome, multiple endocrine neoplasia type 2 (MEN2), involves medullary carcinoma of the thyroid gland. In 2002 there were 10 cases of thyroid cancer per 100 000 population. During the past 10 years the rate of thyroid cancer has been increasing 5% per year. The overall 10-year survival for papillary carcinoma is 80% to 90%, follicular carcinoma 65% to 75%, and medullary carcinoma 60% to 70%. The prognosis for anaplastic carcinoma is very poor and 5-year survival is rare. The dentist by inspection and palpation of the neck in the area of the thyroid gland may detect single or multiple lesions that may be benign or malignant. Patients with identified nodules or enlarged thyroid glands should be referred for diagnosis and treatment. Patients with thyroid cancer will benefit from the early detection and treatment of their lesions as early detection can lead to a cure or prolongation of their life. (*Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006;102:275-80)

The purpose of this paper, part III of the series on thyroid disorders, is to discuss neoplastic lesions of the thyroid gland that may be found in patients presenting for dental treatment. The dentist by inspection and palpation of the neck in the area of the thyroid gland may detect early signs and symptoms of thyroid adenoma or cancer and refer the patient for medical evaluation and treatment. In some cases, this may be lifesaving, whereas in others the quality of life can be improved and complications of thyroid cancer avoided.<sup>1-5</sup>

### THYROID GLAND

The thyroid gland, located in the anterior portion of the neck just below and bilateral to the thyroid cartilage, develops from the thyroglossal duct and portions

of the ultimobranchial body.<sup>1,5,6</sup> The thyroid consists of 2 lateral lobes connected by an isthmus. The right lobe is normally larger than the left,<sup>7</sup> and in some individuals a superior portion of glandular tissue, or pyramidal lobe, can be identified. Thyroid tissue may be found anywhere along the path of the thyroglossal duct, from its origin (midline posterior portion of the tongue) to its termination (thyroid gland, in the neck).<sup>1,5</sup> In rare cases the entire thyroid is found in the anterior mediastinal compartment, however in most individuals the remnants of the duct atrophy and disappear.<sup>6</sup> The thyroglossal duct passes through the region of the developing hyoid bone, and remnants of the duct can become enclosed or surrounded by the bone.<sup>7</sup> Ectopic thyroid tissue may secrete thyroid hormones or become cystic (Fig 1) or neoplastic.<sup>8</sup> In a few individuals, the only functional thyroid tissue is in these ectopic locations.<sup>6</sup>

The parathyroid glands develop from the third and fourth pharyngeal pouches and become embedded in the thyroid gland.<sup>5</sup> Neural crest cells from the ultimobranchial branchial body give rise to thyroid medullary C cells that produce calcitonin, a calcium-lowering

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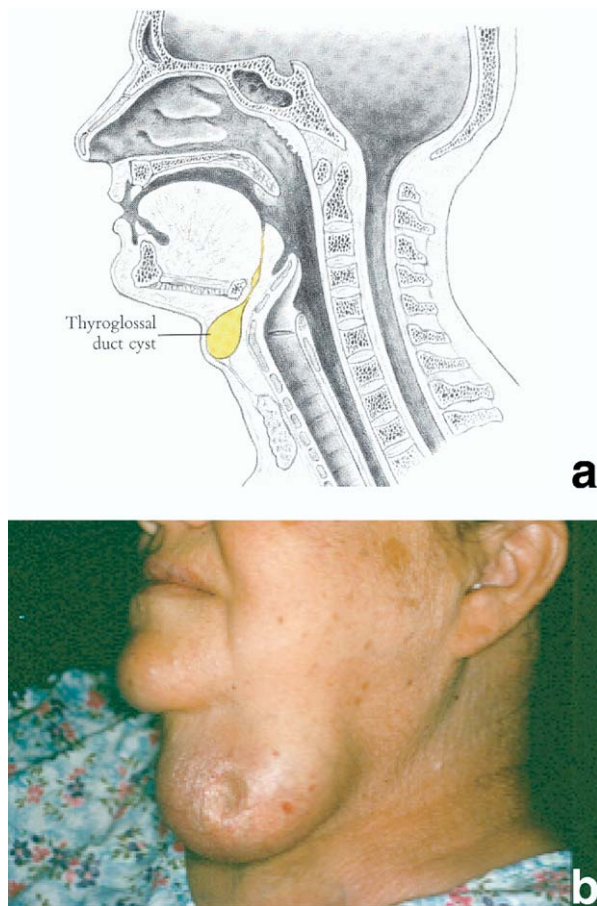


Fig 1. A, The thyroglossal duct originates on the dorsum of the posterior tongue and migrates down the neck to give rise to the thyroid gland. (With permission from Seidel HM, Ball JW, Dains JE, Benedict GW. *Mosby's guide to physical examination*. 3rd ed. St Louis: Mosby; 1995. p. 230.) B, Midline, freely movable cystic mass (thyroglossal duct cyst) in the midline of the neck developed from remnants of the thyroglossal duct.

hormone.<sup>5,6</sup> The C cells are found throughout the thyroid gland.<sup>5,6</sup> In certain neoplastic syndromes the medullary C cells become cancerous.<sup>9</sup>

### THYROID ADENOMAS

Thyroid tumors are the most common endocrine neoplasms.<sup>4</sup> Most of these tumors are benign hyperplastic or colloid nodules or benign follicular adenomas (Fig 2).<sup>4</sup> However, 5% to 10% of the lesions that come to medical attention are carcinomas.<sup>4</sup> A major clinical challenge is establishing which nodules are hyperplastic, benign, or malignant.<sup>4</sup> Ultrasound studies have suggested that the prevalence of nodular lesions of the thyroid is 40% to 60%.<sup>4</sup> It is clear that most of these lesions are benign and do not progress to clinical tu-

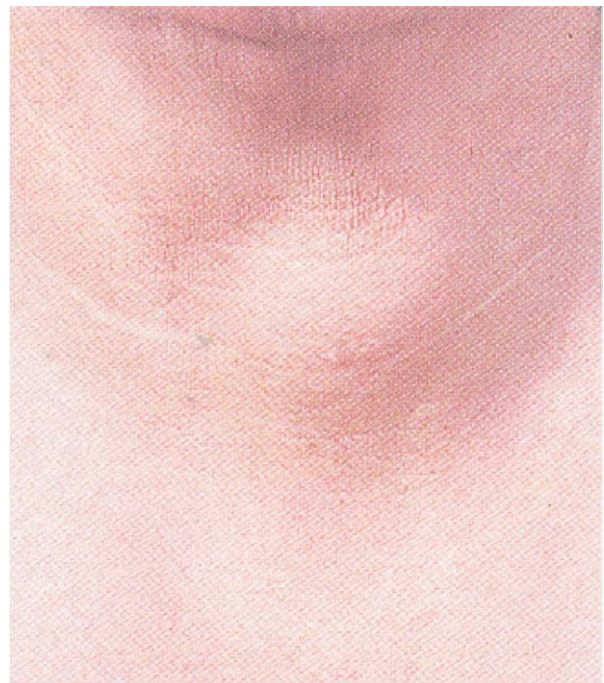


Fig 2. Firm, nontender nodule associated with the thyroid gland. Diagnosed as a thyroid adenoma. (With permission from Forbes CD, Jackson WF. *Color atlas and test of clinical medicine*. 3rd ed. St Louis: Mosby; 2003. p. 310.)

mors.<sup>4</sup> By a thorough history, a careful physical examination, and, when indicated, laboratory testing, imaging procedures and fine-needle aspiration biopsy the malignant lesions can be identified.<sup>4</sup> Clinical findings that favor a benign lesion are a history of Hashimoto's thyroiditis, goiter, or benign thyroid nodule; symptoms of hypothyroidism or hyperthyroidism; and a sudden increase in the size of the nodule with pain or tenderness (cyst or localized thyroiditis).<sup>4</sup>

### THYROID CANCER

There are 3 main histologic types of thyroid cancer: differentiated, medullary, and anaplastic. Differentiated cancers are subdivided into papillary, follicular, and Hurthle cell carcinomas (Table I).<sup>3-5,10</sup> In addition, primary lymphomas may occur in the thyroid gland and other cancers may metastasize to the thyroid. An important neoplastic syndrome, multiple endocrine neoplasia type 2 (MEN2), involves the thyroid gland. MEN2 consists of medullary thyroid carcinoma (MTC), pheochromocytoma in 50% of the cases, and parathyroid hyperplasia/adenoma in 10% to 35% of the cases.<sup>4</sup> In rare cases cancer from other locations may metastasize to the thyroid gland.<sup>11</sup> The kidney is the most common site of origin for metas-

**Table I.** Classification prognosis of thyroid cancer<sup>2,3,10</sup>

Type	Frequency, %	10-year survival, %
Papillary	75-80	80-90
Follicular	8-10	65-75
Hurthle cell	1	60-70
Anaplastic	1-5	<2
Medullary	5-8	60-70
Lymphoma	1-5	45
Metastases to the thyroid	<1	Determined by primary

tasis to the thyroid gland; other sites include breast, lung, and melanoma.<sup>4,11</sup>

**Incidence, prevalence, and demographics**

The frequency of cancer in solitary thyroid nodules has been reported to be about 1% to 5%. Thyroid cancer is found in 8% to 20% of surgically removed thyroid nodules. In autopsy studies of thyroid nodules, about 3% are cancerous.<sup>12,13</sup> The estimated number of cases of thyroid cancer in the United States in the year 2000 was 18 400, with 75% of cases occurring in women.<sup>14</sup> In 2001 there were 19 500 cases of thyroid cancer reported and about 1200 deaths due to thyroid cancer.<sup>2</sup> In 2002 there were 10 cases of thyroid cancer per 100 000 population.<sup>9</sup> During the past 10 years the rate of thyroid cancer has been increasing 5% per year.<sup>9</sup> The overall incidence of thyroid cancer also is rising worldwide.<sup>9</sup> There are more papillary carcinomas occurring but fewer follicular and anaplastic carcinomas.<sup>4</sup>

Differentiated cancers can occur at any age with the median age at diagnosis being 45 to 50 years.<sup>4</sup> Anaplastic cancers are usually found in individuals 60 years of age or older.<sup>4</sup> Differentiated cancers are 3 times more common in women than men.<sup>4</sup> However, over the age of 50 the incidence is the same for men and women.<sup>4</sup> Thyroid cancer is uncommon in children and represents only about 3% of pediatric malignancies.<sup>15</sup>

There appears to be a familial component for papillary carcinoma.<sup>3-5,10</sup> Families with adenomatous polyposis show an increased incidence of papillary cancer and a much higher female-to-male ratio (8:1) and cancers that develop at a younger age.<sup>4</sup> Patients with Cowden’s syndrome (hamartomatous polyps of the stomach, small intestine, and colon; fibrocystic disease and cancer of the breast; and trichilemmomas around the eyes, nose, and mouth) develop thyroid cancer.<sup>4</sup> MEN2 carriers develop MTC and express mutations of the RET proto-oncogene.<sup>4</sup>

Thyroid cancer is more common in areas with endemic goiter.<sup>4</sup> The highest incidence of thyroid cancer is found in Hawaii and the Polynesian islands.<sup>4</sup> Poland has one of the lowest incidences of thyroid cancer.<sup>4</sup>

**Etiology**

External radiation to the cervical region is associated as a cause of thyroid cancer.<sup>4</sup> Children who had thymic irradiation are at increased risk. Teenagers with acne that was treated by irradiation also are at greater risk for thyroid cancer. Patients with other types of neck cancer treated by irradiation have increased risk for thyroid cancer.<sup>4</sup> Children exposed to radioactive fallout from Chernobyl have been found to have an increase in thyroid cancer.<sup>4</sup> External medical diagnostic radiation can add to the risk for thyroid cancer, however dental radiographs do not appear to add to this burden.<sup>4</sup> Radiation to the thyroid from internal sources and diagnostic or therapeutic doses of <sup>131</sup>I have not been associated with an increased risk for thyroid cancer.<sup>4</sup> Environmental factors such as high dietary iodine intake (papillary cancer) or a very low iodine intake (follicular cancer) appear to increase the risk for thyroid cancer.<sup>4</sup> A genetic factor is suggested by an increased risk for thyroid cancer when a family member has had thyroid cancer or MEN2.<sup>3-5,10</sup> In some cases no risk factor can be identified.

**Clinical findings**

On physical examination, manifestations of thyroid malignancy should be sought, including firm consistency of the nodule, irregular shape, fixation to underlying or overlying tissues, and suspicious regional lymphadenopathy.<sup>3-5,10</sup> Signs and symptoms that may be associated with thyroid cancer are a lump in the region of the gland, a dominant nodule(s) in multinodular goiter, a hard painless mass, fixation to adjacent structures, enlarged cervical lymph nodes, a rapidly growing mass, hemoptysis, dysphagia, stridor, and hoarseness.<sup>4</sup>

**Laboratory tests**

The serum thyroid-stimulating hormone (TSH) level is measured to exclude thyroid dysfunction.<sup>3-5,10</sup> However, patients with thyroid cancer rarely have abnormalities in serum TSH levels.<sup>4</sup> A low TSH level (suppressed) may indicate a toxic nodule and should lead to thyroid scintigraphy.<sup>4</sup> In cases of chronic autoimmune thyroiditis, clinical findings may simulate either a solitary nodule or bilateral nodules.<sup>4</sup> In these cases measurement of serum anti-thyroid peroxidase (TPO) antibody and anti-thyroglobulin (Tg) antibody levels may be helpful in the diagnosis of chronic autoimmune thyroiditis.<sup>4</sup> Follicular cell-derived thyroid cancers may release Tg into the blood stream.<sup>4</sup> A number of benign conditions also may release Tg, thus its measurement is not useful in the workup nodular thyroid disease.<sup>4</sup> Serum calcitonin levels are increased in just about all patients with MTC.<sup>3-5,10</sup> It is not cost-effective to mea-



Fig 3. Fine-needle aspiration of a thyroid nodule is the investigation of choice in a patient with a solitary nodule of the thyroid. It is very successful in obtaining cells for cytological examination, which can diagnosis thyroid cancer if present. (With permission from Forbes CD, Jackson WF. Color atlas and text of clinical medicine. 3rd ed. St Louis: Mosby; 2003. p. 313.)

sure calcitonin levels in patients with nodular thyroid disease in the absence of a strong clinical suspicion of MTC.<sup>4</sup>

More than 95% of familial MTC cases have a germline mutation of the RET proto-oncogene that is located on the long arm of chromosome 10.<sup>4</sup> This represents about 4% to 6% of all cases of MTC. When a mutation is found, family members at risk are tested to identify affected individuals. A negative result requires no additional testing. Family members with the mutation should have a prophylactic total thyroidectomy to prevent later development of multicentric MTC.<sup>4</sup>

Ultrasonography also is used to detect thyroid lesions.<sup>9</sup> Nodules 1 to 2 mm in size can be identified. The technique also is used to distinguish solid from cystic lesions, measure the size of the gland, and guide needles for aspiration of cysts or biopsy of thyroid masses.<sup>3-5,10</sup>

The backbone for the diagnosis of thyroid nodules is ultrasonography and fine-needle aspiration biopsy (FNAB).<sup>3-5,10</sup> Clinically detected nodules should be evaluated using ultrasonography. Hypoechoic nodules should be submitted to FNAB (Fig 3). Ultrasound also can be used in cases of nonpalpable nodules to guide FNAB. The overall rates of sensitivity and specificity for FNAB of thyroid nodules exceed 90% in iodine-sufficient areas.<sup>3-5,10</sup> FNAB is easy to perform and safe with very few complications having been reported.<sup>4</sup> The key to the accuracy for the technique is to obtain an adequate specimen. This usually involves obtaining 3 to 6 aspirations that will contain at least 5 or 6 groups of 10 to 15 well-preserved cells.<sup>4</sup> Nodules found in patients living in iodine-deficient areas may require surgical removal in order to establish a diagnosis.<sup>4</sup>

Large lesions, greater than 4 cm, should generally be surgically removed for diagnosis because the rate of sampling error with FNAB in these lesions is increased.<sup>4</sup> Also, cysts greater than 4 cm and cysts that recur after aspiration should be surgically removed for diagnosis.

Computed tomography (CT) and magnetic resonance imaging (MRI) are expensive procedures helpful mainly in the postoperative management of patients with thyroid cancer.<sup>3,4</sup> They are used for the preoperative evaluation of larger lesions of the thyroid, greater than 3 cm, that extend beyond the gland into adjacent tissues.<sup>5,6,16</sup> CT scanning and MRI in the initial diagnosis of thyroid malignancy do not provide higher-quality images of the thyroid and cervical nodes than those of ultrasonography. CT examination of the lower central neck is preferable when tracheal or mediastinal invasion is suspected.<sup>4</sup>

### Treatment

For most papillary carcinomas, surgery is the indicated treatment.<sup>3,4,10</sup> Options include lobectomy and total thyroidectomy. The recurrence rate is higher for lobectomy but complications are fewer.<sup>4</sup> Radioiodine ablation of residual thyroid tissue does not improve survival but does allow for interpretation of thyroglobulin levels.<sup>4</sup> Radioiodine ablation is useful in metastatic disease and locally invasive disease or in cases where cervical lymph nodes can't be resected.<sup>4</sup> Levothyroxine suppression to limit thyrotropin stimulation of tumor growth can be used but side effects may be difficult for the patient to deal with.<sup>4</sup>

Treatment of follicular carcinomas involves surgery followed by radioiodine ablation with lifelong thyrotropin suppression using levothyroxine replacement therapy.<sup>3-5,10</sup> Initial surgery may be thyroid lobectomy or total thyroidectomy.<sup>4</sup> Other options are available for minimally invasive disease: lobectomy and levothyroxine suppression of thyrotropin secretion alone and if the cancer recurs the rest of the thyroid is surgically removed and radioiodine scanning for recurrence or radioiodine ablation of the remaining thyroid tissue and radioiodine scanning for recurrence.<sup>4</sup>

Hurthle cell cancers and medullary carcinomas are treated by total thyroidectomy with cervical lymph node dissection.<sup>3-5,10</sup> Patients with medullary carcinomas should have regular monitoring of serum calcitonin for evidence of recurrence.<sup>4</sup> The main objective with anaplastic carcinomas is to control symptoms and airway obstruction.<sup>4</sup> Any combination of surgery, external beam radiotherapy, and chemotherapy may be used. However, at best these treatments occasionally may add several months to the lifespan.<sup>4</sup> External beam radiotherapy is used to manage bony pain from metastases.<sup>4</sup>

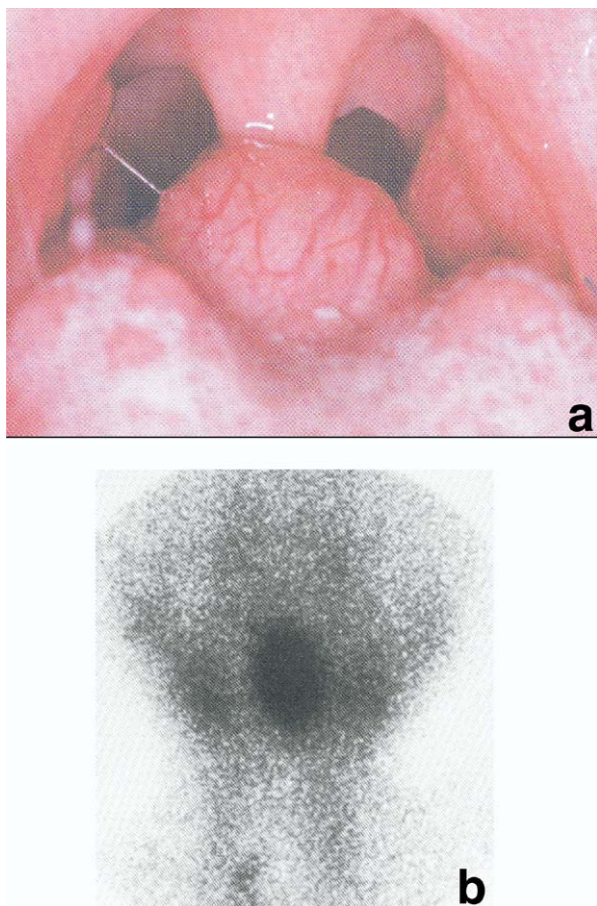


Fig 4. A, Large lingual tumor found on the dorsal posterior aspect of the tongue in a 4-year-old child. B, Thyroid scan of the lesion showing functional thyroid tissue. (With permission from Neville BW. *Oral & maxillofacial pathology*. 2nd ed. Mosby; 2002. p. 720.)

The complications associated with total or subtotal thyroidectomy are hypoparathyroidism, recurrent laryngeal nerve damage, hemorrhage, and the general risks of surgery.<sup>3-5,10</sup> Complications of external beam radiotherapy include damage to the spinal cord, skin damage, and mucosal ulceration.<sup>4</sup> The complications associated with chemotherapy include nausea and vomiting, mucosal damage, hair loss, infection, and bleeding.<sup>4</sup>

### Prognosis

The best prognosis for differentiated cancers is based on age, metastases, and extent and size of the lesion. The best outlook is for young people with localized cancers that are less than 2 cm in size.<sup>4</sup> The overall 10-year survival for papillary carcinoma is 80% to 90%, follicular carcinoma 65% to 75%, and medullary carcinoma 60% to 70%.<sup>4</sup> Involvement of

cervical nodes predicts recurrence in older patients (over 45 years), but not overall survival. Patients with distant metastases of a differentiated carcinoma still have a long-term survival of 43%. The prognosis for anaplastic carcinomas is very poor and 5-year survival is rare (Table I).<sup>4</sup>

### Dental management

Palpation and inspection of the thyroid gland should be part of the routine head and neck examination performed by the dentist. The anterior neck region can be scanned for indications of old surgical scars; the posterior dorsal region of the tongue should be examined for a nodule that could represent lingual thyroid tissue; and the area just superior and lateral to the thyroid cartilage should be palpated for the presence of a pyramidal lobe. Although difficult to detect, the normal thyroid gland can be palpated in many patients.<sup>2,5</sup> It may feel rubbery and may be more easily identified by having the patient swallow during the examination.<sup>1</sup> As the patient swallows, the thyroid rises; lumps in the neck that may be associated with it also rise (move superiorly). Nodules related to the thyroglossal duct (thyroglossal duct cysts) move upward with protrusion of the patient's tongue.<sup>1</sup>

If a thyroid enlargement is noted, even though the patient appears euthyroid (normal thyroid function), a referral should be made for evaluation before dental treatment is rendered. A diffuse enlargement may be simple goiter, subacute thyroiditis, or chronic thyroiditis. The patient may be hyperthyroid, hypothyroid, or euthyroid. Isolated nodules may turn out to be a cyst, adenoma, or carcinoma. Growing nodules in diffusely enlarged glands or in glands with multinodular involvement may represent thyroid carcinoma and need to be evaluated by a physician.<sup>1</sup>

An enlarged thyroid gland caused by hyperplasia (goiter) feels softer than the normal gland. Adenomas and carcinomas involving the gland are firmer on palpation and are usually seen as isolated swellings.<sup>2,5</sup> Patients with Hashimoto's disease or Riedel's thyroiditis have a much firmer gland on palpation than the normal gland.<sup>17</sup>

A physician should evaluate a patient found to have a dorsal, posterior, or lingual tumor that is euthyroid before the mass is surgically removed (Fig 4). This usually is done by radioactive iodine scanning.<sup>6,18</sup>

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