1.2. THYROID AND PARATHYROID PHYSIOLOGY

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The purpose of this chapter is to review the details of thyroid anatomy and physiology that facilitate an understanding of thyroid cancer management.

EMBRYOLOGY

The thyroid is embryologically derived from the primitive foregut and neural crest cells. The gland is comprised of two types of secretory cells: follicular cells that arise from the embryonic foregut and C cells that are derived from the neural crest (Santisteban 2005). These two cell types, respectively, synthesize thyroid hormone and calcitonin, the two main classes of hormones in the gland. The functional subunits of the thyroid are sphere-shaped follicles that contain an intra-luminal pool of colloid. Cuboidal follicular cells that synthesize and secrete thyroid hormones make up the lining of each follicle (Fig. 1). A thin layer of connective tissue containing a dense network of capillary and lymphatic vessels separates the follicles from each other. Within the interfollicular connective tissue, and interspersed among the follicular cells, are the thyroidal C cells that synthesize calcitonin.

THYROID HORMONE

The thyroid gland produces two biologically active forms of thyroid hormone: thyroxine (3, 5, 3’, 5’ iodothyronine or T4) and triiodothyronine (3, 5, 3’ iodothyronine or T3) (Engler 1984). Both contain an outer phenyl ring and an inner tyrosine ring attached by an ether linkage (Fig. 2). Conceptually it is useful to think of T4 as the
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Parafollicular (C) Cell

Follicle (Thyroglobulin)

Follicular Cells

Figure 1. Thyroid follicle. Thyroid follicular cells produce thyroglobulin and thyroid hormone. Thyroid C cells, synthesize and secrete calcitonin.

storage and transport form of thyroid hormone and T3 as the metabolically active form. Most (∼80%) thyroid hormone in the thyroid gland and plasma is T4, which is rapidly converted to T3 in skeletal muscle, liver, brain and other tissues by removal of an outer ring 5’ iodine molecule. T3, and to a much smaller extent T4 (which acts mainly as a prohormone), are bound to specific nuclear receptors in peripheral cells that interact with regulatory regions of genes, influencing their expression. The tissue concentration of T3 almost completely determines the biologic effect of thyroid hormone. Levothyroxine (T4) alone is effective thyroid hormone replacement therapy because T3 is almost exclusively derived from T4.

IODINE AND THYROID FUNCTION

Iodine is essential for normal thyroid function (Fig. 2). The minimum daily intake necessary to prevent iodine deficiency goiter is 50 μg and the recommended daily intake is 150 μg. Urinary iodine is a reflection of iodine intake. Urinary iodine level was about 600 to 700 μg/L per day in the U.S. a few years ago but has been falling in recent years and now averages only about 150 μg/L (Hollowell 1998; Hollowell 2002).