The thyroid gland produces thyroid hormone, which has clinically important actions practically in every system in the human body. Detailed knowledge of the physiology of the thyroid gland is critical for the proper management of thyroid disorders. The molecular biology of thyroid function is being studied in great detail. Clinically important molecules, such as the thyroid-stimulating hormone receptor and the sodium/iodide symporter, have been identified and well characterized. Such discoveries have significantly improved our understanding of thyroid physiology. As a result, new diagnostic and therapeutic approaches for the management of thyroid disorders are now available or in development.

Hyperthyroidism describes the sustained increase in thyroid hormone biosynthesis and secretion by a thyroid gland with increased metabolism. Although the use of radioiodine scanning serves as a useful surrogate that may help characterize the cause of thyrotoxicosis, it only indirectly addresses the underlying physiologic mechanism driving the increase in serum thyroid hormones. In this article, thyrotoxic states are divided into increased or decreased thyroid metabolic function. In addition to the diagnosis, clinical presentation, and treatment of the various causes of hyperthyroidism, a section on functional imaging and appropriate laboratory testing is included.

Hypothyroidism is the result of inadequate production of thyroid hormone or inadequate action of thyroid hormone in target tissues. Primary hypothyroidism is the principal manifestation of hypothyroidism, but other causes include central deficiency of thyrotropin-releasing hormone or thyroid-stimulating hormone (TSH), or consumptive hypothyroidism from excessive inactivation of thyroid hormone. Subclinical hypothyroidism is present when there is elevated TSH but a normal free thyroxine level. Treatment involves oral administration of exogenous synthetic thyroid hormone. This review presents an update on the etiology and types of hypothyroidism, including subclinical disease; drugs and thyroid function; and diagnosis and treatment of hypothyroidism.

Subacute, silent, and postpartum thyroiditis are temporary forms of thyroid dysfunction caused by thyroid gland inflammation. They classically
present with a triphasic course: a brief period of thyrotoxicosis due to release of preformed thyroid hormone that lasts for 1 to 3 months, followed by a more prolonged hypothyroid phase lasting up to 6 months, and eventual return to a euthyroid state. However, the types and degree of thyroid dysfunction are variable in these disorders, and individual patients may present with mild or more severe cases of thyrotoxicosis alone, hypothyroidism alone, or both types of thyroid dysfunction.

Thyroid Disorders During Pregnancy

Cynthia F. Yazbeck and Shannon D. Sullivan

Thyroid disorders are common in women during pregnancy. If left untreated, both hypothyroidism and hyperthyroidism are associated with adverse effects on pregnancy and fetal outcomes. It is important to correctly identify these disorders and treat them appropriately to prevent pregnancy-related complications. Levothyroxine is the indicated treatment for hypothyroidism, and thionamides are the treatment of choice for hyperthyroidism; thyroidectomy may be indicated in select cases. When thyroid cancer is diagnosed during pregnancy, a decision must be made regarding performing thyroidectomy during the pregnancy or postponing surgical resection until the postpartum period. Radioactive iodine is absolutely contraindicated during pregnancy and lactation.

Thyroid Hormone and the Cardiovascular System

Sara Danzi and Irwin Klein

Thyroid hormone has profound effects on the heart and cardiovascular system. This article describes the cellular mechanisms by which thyroid hormone acts at the level of the cardiac myocyte and the vascular smooth muscle cell to alter phenotype and physiology. Because it is well established that thyroid hormone, specifically T₃, acts on almost every cell and organ in the body, studies on the regulation of thyroid hormone transport into cardiac and vascular tissue have added clinical significance. The characteristic changes in cardiovascular hemodynamics and metabolism that accompany thyroid disease states can then be best understood at the cellular level.

The Effect of Thyroid Disorders on Lipid Levels and Metabolism

Leonidas H. Duntas and Gabriela Brenta

Thyroid hormones regulate cholesterol and lipoprotein metabolism, whereas thyroid disorders, including overt and subclinical hypothyroidism, considerably alter lipid profile and promote cardiovascular disease. Good evidence shows that high thyroid-stimulating hormone (TSH) is associated with a non-favorable lipid profile, although TSH has no cutoff threshold for its association with lipids. Thyromimetics represent a new class of hypolipidemic drugs: their imminent application in patients with severe dyslipidemias, combined or not with statins, will improve the lipid profile, potentially accelerate energy expenditure and, as a consequence, vitally lessen the risk of cardiovascular disease.
The Effect of Medications on Thyroid Function Tests
Priya Kundra and Kenneth D. Burman

Drug-induced thyroid disorders are common in clinical practice. It is important to recognize the various drugs contributing to thyroid dysfunction for a timely intervention to help achieve a euthyroid state. The pathways of thyroid hormone synthesis, secretion, transport, metabolism, and absorption offer numerous targets for medication interactions. This article discusses some of the medications that may influence thyroid function tests.

Approach to and Treatment of Thyroid Disorders in the Elderly
Maria Papaleontiou and Megan R. Haymart

Thyroid gland dysfunction is prevalent in older adults and may be associated with significant morbidity if misdiagnosed and left untreated. Because of a decreased number of symptoms at presentation, an increased susceptibility to adverse events if not treated, and a greater likelihood of harm from treatment, the diagnosis and management of thyroid disorders in older adults can be challenging. This review focuses on the epidemiology, clinical presentation, risks and complications, and management of thyroid disorders in older adults, including hyperthyroidism, hypothyroidism, thyroid nodules, and thyroid cancer.

The Evaluation and Treatment of Graves Ophthalmopathy
Marius N. Stan, James A. Garrity, and Rebecca S. Bahn

Optimum care of the patient with Graves ophthalmopathy (GO) is achieved through teamwork between the endocrinologist and ophthalmologist, with input from ancillary specialists as needed. Clinical evaluation should include determination of both the severity and the activity of the disease. It is important to assess early in the evaluation the impact of the disease on the patient’s quality of life and their priorities and expectations regarding management. Once this information has been gathered, careful discussion between patient and physicians can define the management plan. This article reviews the pathophysiology, epidemiology, evaluation, and management of GO.

Thyroid Nodules
Geanina Popoveniuc and Jacqueline Jonklaas

Thyroid nodules are common entities, clinically important primarily because of their malignant potential. Serum thyrotropin and thyroid ultrasonography are pivotal in evaluating thyroid nodules. Fine-needle aspiration biopsy is the most accurate tool for diagnosing malignancy and selecting candidates for surgery. An approach to the initial evaluation and management of single nodules, functioning nodules, multinodular glands, incidental nodules, and cysts is discussed, as are therapeutic interventions for benign nodules. Thyroid cancer discovered during pregnancy is also discussed.
Approach to and Treatment of Goiters

Geraldo Medeiros-Neto, Rosalinda Y. Camargo, and Eduardo K. Tomimori

The main causes of simple diffuse goiter (SDG) and multinodular goiter (MNG) are iodine deficiency, increase in serum thyroid-stimulating hormone (TSH) level, natural goitrogens, smoking, chronic malnutrition, and lack of selenium, iron, and zinc. Increasing evidence suggests that heredity is equally important. Treatment of SDG and MNG still focuses on L-thyroxine-suppressive therapy surgery. Radioiodine alone or preceded by recombinant human TSH stimulation is widely used in Europe and other countries. Each of these therapeutic options has advantages and disadvantages, with acute and long-term side effects.

Approach to and Treatment of Differentiated Thyroid Carcinoma

Furio Pacini and Maria Grazia Castagna

Thyroid cancer is the most common endocrine malignancy, although representing fewer than 1% of all human tumors. Differentiated thyroid carcinoma (DTC) includes the papillary and follicular histotypes and their variants, accounting for more than 90% of all thyroid cancers. Given the changing presentation of DTC in the last years, the aim of DTC management is to ensure the most effective but least invasive treatment, and adequate follow-up for a disease that nowadays is mostly cured just with surgery and is rarely fatal. This review addresses the multiple steps of current management, based on previous assumptions.

Thyroid Emergencies

Joanna Klubo-Gwiezdzinska and Leonard Wartofsky

This review presents current knowledge about the thyroid emergencies known as myxedema coma and thyrotoxic storm. Understanding the pathogenesis of these conditions, appropriate recognition of the clinical signs and symptoms, and their prompt and accurate diagnosis and treatment are crucial in optimizing survival.

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