Graves’ Disease

Named after Irish physician Robert Graves, a man who was not, in fact, the original discoverer of the disease, Graves’ Disease is the most common cause of hyperthyroidism in North America. It is an autoimmune disorder where antibodies are formed against TSH-R, thyroglobulin and thyroid peroxisome, among other molecules. Although the stimulus that triggers this process is unknown, it is suspected that the disease begins with a loss of helper T-cell tolerance; bacterial and viral infections, the post-partum state, lithium therapy, stress, interferon alpha and iodine excess have been postulated causes of the onset of Graves’. Thyroid-stimulating immunoglobulin, an IgG antibody, stimulates TSH-R, causing excessive release of thyroid hormone. Thyroid growth-stimulating immunoglobulins (TGIs) also engage the TSH-R and cause follicular epithelial proliferation while TSH-binding inhibitor immunoglobulins (TBIIs) are anti-TSH-R antibodies that can either mimic TSH or inhibit thyroid cell function, causing periods of hypothyroidism. The disease predominantly affects women, is present in up to 1.5 to 2% of women in the United States, and possesses a strong familial association. HLA-B8 and HLA-DR3 have been associated with Graves’, as have other markers.

Symptoms of Graves’ involve many organ systems, and can include tremor, lid lag, tachycardia, sweating, weight loss, diarrhea and heat intolerance. Younger and older patients can have slightly different findings: In the young, bone growth occurs quickly and with early bone maturation while the elderly may experience cardiovascular complications including heart failure. Graves’ is associated with a wide range of ocular pathology, including exopthalmos, ophthalmopathy, periorbital edema, and keratitis. Blindness may result when the disease involves the optic nerve. The exophthalmos is caused by glycosaminoglycan accumulation as well as cellular infiltration of the ocular muscles and tissues, and swelling of the extraocular tissue. Characteristic physical signs of Graves’ also include diffuse goiter, muscle weakness, and pretibial myxedema. The skin findings are due to glycosaminoglycan accumulation. Histologically, the gland becomes hyperplastic with minimal colloid and a columnar epithelium.

While eye findings are indicative of Graves’, in their absence, TSH testing as well as a radiiodine test are used as diagnostic tools. Patients with Graves’ will demonstrate diffuse enlargement of the gland, increased iodine uptake and TSH suppression; early Graves’ will demonstrate elevated T3 levels. Another finding diagnostic of Graves’ is elevated TSH-R or thyroid-stimulating antibody. Although non-specific findings, Graves’ may also present with elevated anti-TPO or anti-thyroglobulin (anti-Tg). While Graves’ Disease accounts for a majority of the instances of thyrotoxicosis, Graves’ and other states of hyperthyroidism should not be confused with the disorder, defined as an excess of thyroid hormone. Hyperthyroidism is diagnosed by testing the TSH level; it should be
depressed, regardless of whether the T4 or T3 levels are elevated. Radioiodine scans will show a diffuse uptake of iodine and radioactive iodine uptake increases in Graves’.

Treatment of Graves’ is not uniform across all disease sufferers. Younger patients may be treated with antithyroid medication including propylthiouracil (PTU) and methimazole, both of which reduce thyroid hormone production. Thyroid ablation using radioactive iodine (131I) or thyroidectomy and subsequent thyroid hormone supplementation are other therapeutic options. Since women of child-bearing age are advised to wait a year after radioactive iodine therapy to attempt to conceive, surgery is recommended instead, as it is for some young patients, patients with thyroid cancer or suspicious nodules, patients with goiters and compressive symptoms, patients with ophthalmopathy and patients allergic to antithyroid medications. Patients with ophthalmopathy run the risk of worsening ocular problems with radioactive ophthalmopathy, while studies have shown total thyroidectomy may stabilize or improve the disease.

References: