Thyroid Antibodies

**Autoimmune Thyroid Disease** – Graves’ hyperthyroidism and Hashimoto’s hypothyroidism (AKA autoimmune thyroiditis) are caused by a T and B-Cell lymphocytic infiltrate that results in the production of auto-antibodies to thyroid gland antigens. These diseases are related not only by a similar pathogenesis, but share a hereditary relationship and have been reported to manifest at different times in the same patient.

**Thyroid Stimulating Immunoglobulins (TSI), TSHR Ab, TR Ab, TBII**
- All names for antibodies to the thyrotropin (TSH) receptor.
- Antibodies can be stimulating or inhibiting. Stimulating antibodies (TSI) are the cause of Graves’ hyperthyroidism. Levels decline in some patients treated with antithyroid meds. Inhibiting antibodies can play a role in Hashimoto’s hypothyroidism.
- The utility of checking TSI to confirm diagnosis of Graves’ or to predict likelihood of relapse is controversial.\(^1\)
- Antibodies should be checked in patients with Graves’ in the third trimester of pregnancy, because high titers are correlated with neonatal hyperthyroidism.
- TSI at SFGH sensitivity of 80% for presence of stimulating antibodies, TSHR – Ab (TBII) at SFGH sensitivity is 90%.

**Thyroid peroxidase antibodies (TPO Ab) AKA microsomal Ab** About 90% of patients with Hashimoto’s have anti-thyroid antibodies and 99% of these have TPO Ab. Often ordered in suspected Graves’ or Hashimoto’s to confirm autoimmune thyroid disease.
- Presence of these antibodies in pregnancy increases the likelihood of post-partum thyroiditis from 10% to 33%.
- Run every Friday at SFGH lab.

**Thyroglobulin antibodies (Tg Ab)** Almost all patients with Hashimoto’s hypothyroidism have high titers. Lower titers are common in patients with other thyroid disease or normals.
- Falling titers are a good prognostic sign during the treatment of thyroid cancers.
- Available at SFGH as a sendout only.

**Sodium-iodide symporter Ab** Present in 0-20% of patients with Hashimoto’s hypothyroidism.

### Prevalence of Antithyroid Antibodies (in percent)\(^2\)

<table>
<thead>
<tr>
<th></th>
<th>TSHR Ab</th>
<th>Tg Ab</th>
<th>TPO Ab</th>
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</thead>
<tbody>
<tr>
<td>General Population</td>
<td>0</td>
<td>5-20</td>
<td>8-27</td>
</tr>
<tr>
<td>Graves’</td>
<td>80-95</td>
<td>50-70</td>
<td>50-80</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>10-20</td>
<td>80-90</td>
<td>90-100</td>
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<tr>
<td>Hashimoto’s</td>
<td></td>
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<tr>
<td>Hypothyroidism</td>
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<tr>
<td>Relatives of patients</td>
<td>0</td>
<td>40-50</td>
<td>40-50</td>
</tr>
</tbody>
</table>

**Pearls:**
- Patients with subclinical hypothyroidism (elevated TSH, normal T4) AND thyroid antibodies (TPO or Tg Ab) are twice as likely to progress to overt hypothyroidism.
- TSI-positive, TPO-negative patients are particularly at-risk for Graves ophthalmopathy.\(^3\)
- *Lid lag and stare* – Due to hyperthyroidism, ie direct action of thyroid hormone on the levator palpebrae muscle.
- *Proptosis* – Due to deposition of glycosaminoglycans in extraocular muscles and orbital adipose tissue from the inflammation likely caused by TSHR antibodies to the TSH receptor that is expressed in these tissues.
Thyroid hormone biosynthesis  Thyroid hormone synthesis includes the following steps: (1) iodide (I) trapping by the thyroid follicular cells; (2) diffusion of iodide to the apex of the cells; (3) transport of iodide into the colloid; (4) oxidation of inorganic iodide to iodine and incorporation of iodine into tyrosine residues within thyroglobulin molecules in the colloid; (5) combination of two diiodotyrosine (DIT) molecules to form tetraiodothyronine (thyroxine, T4) or of monoiodotyrosine (MIT) with DIT to form triiodothyronine (T3); (6) uptake of thyroglobulin from the colloid into the follicular cell by endocytosis, fusion of the thyroglobulin with a lysosome, and proteolysis and release of T4, T3, DIT, and MIT; (7) release of T4 and T3 into the circulation; and (8) deiodination of DIT and MIT to yield tyrosine. T3 is also formed from monodeiodination of T4 in the thyroid and in peripheral tissues. (Modified from Scientific American Medicine, Scientific American, New York, 1995.)

Autoantibody targets
1. Location of Na-I symporter
4. Thyroglobulin
6. TPO or microsomal Ab
* TSH receptor

Sources: Up To Date: Pathogenesis and clinic features of Graves’ ophthalmopathy, Pathogeneisis of Graves Disease
SFGH Lab Medicine Manual 2002 Labcorp.com
3 Khoo et al. The combination of absent TPO Ab and high TSI levels... Thyroid 1999; 9:1175-80.