



Thyroid Function

Thyroid Antibodies

Analyte Information





Thyroid Antibodies

Determination of thyroid autoantibodies are, besides TSH and FT4, one of the most important diagnostic parameters. Measurement of thyroid antibodies is applied in the diagnosis of thyroid disease of autoimmune origin. Thyroid autoantibodies can be divided into several groups. The most frequent are antibodies against thyroglobulin (anti-Tg) and antibodies against thyroid peroxidase (anti-TPO). Another group consists of antibodies against the TSH receptor (anti-rTSH), antibodies against thyroid hormones, and antibodies against some other surface structures of thyrocytes. Autoantibodies have the heterogeneous character and may change with time. Human immune system produces the various types of these antibodies with different binding affinity to the antibodies used in immunoassays. Therefore, the correlation between the level and the activity of these antibodies may be poor. The presence of thyroid antibodies is more likely to be found in patients with other autoimmune diseases than in general population.

Thyroglobulin Antibodies

Introduction

Thyroglobulin (Tg) is a big dimeric protein consisting of two identical subunits. It has 2,748 amino acids in total, and a molecular weight (Mr) of approximately 670 kDa. Thyroglobulin is the site of T3 and T4 synthesis. Thyroglobulin antibodies (anti-Tg) are polyclonal IgG antibodies. Anti-Tg are directed against the Tg protein, a major constituent of thyroid colloid. Anti-Tg antibodies may be present in approx. 10-20% of the general population and in approx. 25% of thyroid cancer patients. In Hashimoto's thyroiditis, immunocytes invade the thyroid gland and synthesize antibody to thyroglobulin. The autoantibodies gradually destroy the thyroid hormones, causing hypothyroidism.


Clinical application

The presence of anti-Tg indicates the autoimmune basis of Hashimoto's thyroiditis or Graves' disease. Anti-Tg are less often present and less pathogenic



than anti-TPO. Anti-Tg can interfere in the assay for thyroglobulin which is used for the monitoring of thyroid cancer patients. Anti-Tg antibodies may cause falsely decreased Tg results in "sandwich" immunoassay methods, and falsely increased results in competitive immunoassay methods. For correct interpretation, it is always necessary to determine anti-Tg antibodies, or to perform a recovery test, in order to exclude the possibility of antibody interference.

Elevated anti-Tg levels

- 
- Hashimoto's thyroiditis
 - Graves' disease
 - idiopathic myxedema
 - nontoxic goitre
 - thyroid cancer
 - pernicious anemia

Levels

The determined levels of anti-Tg differ significantly in dependence on particular assay. For each assay, relevant reference values are given in the appropriate Instructions for Use (IFU). Anti-Tg levels presented in Tab.1 were obtained using Beckman Coulter RIA kit (cat. No. IM3223).

Tab.1: Anti-Tg levels

Specimen (serum)	Reference interval (IU/mL)
Healthy adults	0 - 30
Positive	> 30



Thyroid Peroxidase Antibodies


Introduction

The thyroid peroxidase occurs in thyroid cell microsomes and is responsible for oxidation of iodide to iodine and for other steps important in T3 and T4 synthesis. The antibodies against thyroid peroxidase (anti-TPO) are a secondary response to thyroid injury. Anti-TPO are polyclonal IgG antibodies and present amounts correlate with lymphocytic infiltration of thyroid. Anti-TPO levels also correlate with thyroid damage.

Clinical application

The main indication for anti-TPO determination is to evaluate if the thyroid dysfunction is caused by autoimmune process in thyroid gland, either Hashimoto's or Graves' disease, or by some other form of thyroid failure. Anti-TPO and anti-Tg can occur together in many cases. One or both antibodies are found in almost 100% of patient with autoimmune. Anti-TPO has higher affinity and is usually present in higher levels than anti-Tg. An increase of anti-TPO may be an indication to start treatment with thyroxine in patients with subclinical hypothyroidism with an elevated TSH and normal FT4. The progression to overt thyroid failure occurs at the rate of 5% per year. About 50% of women with anti-TPO positivity in early pregnancy will to develop some form of postpartum thyroid dysfunction. Clinically healthy people with anti-TPO positivity need more frequent monitoring of their thyroid function.

Elevated anti-TPO levels

- 
- Hashimoto's thyroiditis
 - Graves' disease
 - asymptomatic individuals



Levels

The determined levels of anti-TPO differ significantly in dependence on particular assay. For each assay, relevant reference values are given in the appropriate Instructions for Use (IFU). Anti-TPO levels presented in Tab.2 were obtained using Beckman Coulter RIA kit (cat. No. A56719).

Tab.2: Anti-TPO levels

Specimen (serum)	Reference interval (IU/mL)
Healthy adults	0 - 12
Positive	> 12

Thyrotropin Receptor Antibodies

Introduction

Thyrotropin receptor antibodies (anti-rTSH) are group of related immunoglobulins that bind to thyroid cell membranes at or near the TSH-receptor. In general, these antibodies demonstrate substantial heterogeneity. Some anti-rTSH cause thyroid stimulation, whereas others decrease thyroid secretion via blocking of TSH action, and third type of anti-rTSH has no effect on thyroid secretion activity.


Clinical application

The determination of anti-rTSH is useful tool in diagnosis of Graves' disease. Anti-rTSH assay can be also ordered in the case of special problems, as in patients with initial unilateral exophthalmos, or sometimes with subclinical hyperthyreoidism, in hyperemesis with thyreotoxicosis or in the differential diagnosis of postpartum painless thyroiditis. In pregnant women with Graves' disease, transplacental passage of stimulated anti-rTSH from mother to fetus can result in transient neonatal hyperthyroidism. Anti-rTSH should be measured in the last trimester and if high, careful evaluation of the neonate is required to detect hyperthyroidism. In Hashimoto's disease, blocking anti-rTSH



May rarely cross the placenta, causing transient neonatal hypothyroidism.

Elevated anti-rTSH levels

- 
- Graves' disease
 - other autoimmune thyroid disorders
 - toxic nodular goitre

Levels

The determined levels of anti-rTSH differ significantly in dependence on particular assay. For each assay, relevant reference values are given in the appropriate Instructions for Use (IFU). Anti-rTSH levels presented in Tab.3 were obtained using Beckman Coulter RIA kit (cat. No. A15728).

Tab.3: Anti-rTSH levels

Specimen (serum)	Reference interval (U/L)
Healthy adults	> 1
Borderline positive	1.1 – 1.5
Positive	< 1.5

Conclusions

Thyroid antibodies are very specific type of analyte. The current guidelines of medical societies prefer the using of single cut-off value instead of gray zone. The examination strategy has changed during last few years. At present, the levels of thyroid antibodies have diagnostic and prognostic significance. The incidence of antibodies is geographically different. The number of cases with the autoantibodies positivity increases with the age. Anti-TPO positivity almost always precedes the anti-Tg positivity. Recently, a number of studies around the world have shown that high levels of anti-TPO occur in patients with breast cancer and colorectal cancer. Presence of anti-TPO antibodies in euthyroid patients is considered as a risk factor for cancer development.



The presence of antibodies in selected conditions is summarized in the following table.

Tab.4: Occurrence of thyroid antibodies in different conditions

Condition	Occurrence of antibodies (%)		
	anti-TPO	anti-Tg	anti-rTSH
Healthy population	5-20	5-25	0
Hashimoto's thyroiditis	90-100	70-80	15
Graves' disease	70-80	50-60	90
Toxic nodular goitre			15
Thyroid cancer	10-40	30-60	5
Pregnancy	8-14	8-14	
Autoimmune diseases	40	40	10
Diabetes mellitus type 1	40	40	0
Adrenal insufficiency	60	30	0
Pernicious anemia	40	30	0
Rheumatoid arthritis	60	40	0
Breast cancer	50	5	0
Colorectal cancer	40	0	0

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