

## Podcast 32: The Role of IVD To Detect Thyroid Disorders and Ensure Proper Treatment

### **Andrea Ott-Vasconi:**

Hello, I'm Andrea Ott-Vasconi, and welcome to QuidelOrtho Science Bytes. In this episode, we'll be talking about the most common thyroid disorders, how they can be diagnosed and monitored, and complications that can arise if left undetected. According to the American Thyroid Association, more than 12 percent of the U.S. population will develop a thyroid condition during their lifetime, and up to 60 percent of those with thyroid disease are unaware of their condition.

With me today to discuss thyroid diseases and diagnostic testing is Dr. Rea Castro, Director of Medical Affairs at QuidelOrtho. Dr. Castro holds a bachelor's degree in medical technology from the University of San Tomas and a medical degree from the University of the East in the Philippines. In addition, she also has a master's in public health from the Northern Illinois University. She has experience in both clinical and biotechnology product development, covering multiple therapeutic areas. Her clinical focus before going into industry was in women's health. Thank you, Dr. Castro for joining me today.

### **Rea Castro:**

Thank you, Andrea, for having me.

### **Andrea Ott-Vasconi:**

Let's begin with, what are the most common thyroid disease states and their causes?

### **Rea Castro:**

Well, the most common thyroid disease states are due to either overproduction or under production of the thyroid hormones. The thyroid produces two major hormones called T3 or triiodothyronine and T4 or thyroxin. An overproduction of thyroid hormones cause hyperthyroidism. A common cause of hyperthyroidism is an autoimmune disorder called Graves' Disease. Under production of thyroid hormones cause hypothyroidism, an autoimmune disorder called Hashimoto's Thyroiditis is a disease that cause the body's immune system cells to attack the thyroid cells, which then leads to underproduction and is the most common cause of hypothyroidism.

Overgrowth of the thyroid gland can also occur and causes a disorder called goiter and is commonly caused by the lack of iodine in our diets. Goiter can either be hyper- or hypothyroid. Less common thyroid diseases include thyroiditis, thyroid nodules and thyroid cancer. Thyroiditis is an inflammation of the thyroid. Hashimoto's is actually a type of thyroiditis. Other types include postpartum thyroiditis, which is a condition that happens after delivery of the baby and sub-acute thyroiditis, which is a condition causing pain in the thyroid. Thyroid nodules are abnormal growths of thyroid cells that form a lump and are most commonly non-cancerous, but a small proportion may lead to cancer. Cancers in the thyroid is usually due to high levels of radiation, but hereditary factors can also play a role.

### **Andrea Ott-Vasconi:**

Thank you for that overview. What are the symptoms that are associated with each disease?

### **Rea Castro:**

Well, hyperthyroidism accelerates your body's metabolism so symptoms can include nervousness, anxiety, irritability and decreased sleep. You'll notice increased sweating, your heart racing and hand tremors. You'll also notice thinning of your skin and brittle hair. You sometimes will experience muscle

weakness and frequent bowel movements. You'll notice weight loss despite of your healthy appetite, and in women, less frequent and light menstrual periods.

Symptoms of hypothyroidism relate to slowing of your body's metabolism. They tend to develop slowly and you barely notice the symptoms and often attribute it to age such as fatigue, weight gain, dry skin and thinning hair, feeling cold, forgetfulness, depression and constipation.

#### **Andrea Ott-Vasconi:**

And thyroid diseases are amongst the most prevalent of medical conditions. Help us better understand the epidemiology.

#### **Rea Castro:**

So, thyroid diseases are more common in women than men. One in eight women will develop thyroid problems during her lifetime with hypothyroidism more likely to develop after menopause. Thyroid dysfunction in diabetes are also closely linked. Autoimmune thyroid dysfunction occurs in 17 to 30 percent of adults with Type 1 diabetes. Thyroid dysfunction is more common in patients with Type 2 diabetes than in the general population. So the prevalence of thyroid dysfunction really varies by age, sex, race, ethnicity and geography.

There are limitations in the epidemiological studies with current estimates of thyroid dysfunction largely derived from predominantly white and middle age populations. There are also different techniques used to measure thyroid hormones and different definitions used in these studies. In one large cross-sectional study of the US population where all subjects were 65 or older, higher age was significantly associated with higher prevalence of subclinical hypothyroidism. The prevalence of subclinical hypothyroidism was also higher in whites compared to Blacks, whereas the opposite trend was found for subclinical hyperthyroidism where the prevalence is greater in Blacks compared to whites.

So variations in prevalence are influenced by the dietary availability of iodine, which is an essential component of T3 and T4 produced by the thyroid gland. Almost one third of the global population live in areas of iodine deficiency, most of which are in developing countries. However, several high-income countries like Denmark, Italy and the UK have also been classified as iodine deficient. In the U.S., there's been iodine intake decrease over the last 30 years, and surveys suggest that pregnant women in both developing and high-income countries have deficient iodine intakes.

#### **Andrea Ott-Vasconi:**

And there are many different assays used to diagnose the different thyroid disease states. Which ones are used to aid in the diagnosis of the diseases you've described?

#### **Rea Castro:**

So, blood tests can help diagnose thyroid diseases. The different assays available are TSH, free and total T3 and T4, and different types of thyroid antibodies. TSH or thyroid stimulating hormone, is a pituitary hormone that stimulates the thyroid gland to produce T3 and T4 so if this hormone is increased, that means there's too little thyroid hormone, and if it's decreased, there's too much thyroid hormone in the body. This is actually the most common test doctors use in evaluating thyroid function.

Measuring the free or unbound levels of T3 and T4 also helps in this evaluation to determine the degree of hyper or hypothyroidism. Free T4 is usually added if the TSH is high to determine the degree of hypothyroidism. Free T4 and T3 are added when TSH is low to determine the degree of hyperthyroidism. Total T3 and T4 measures both the bound and the free hormones and may not accurately reflect the

condition of the thyroid as much as the free hormones because it is greatly dependent on the amount of binding protein in the blood and can be influenced by many non-thyroid conditions. It is however useful in full assessment because it is a great representation of the overall production capacity of the thyroid gland.

So, if our free hormones are low and the total hormones are also low, this means it is due to issues in production. If the free hormones are low and the total hormones are normal, then it's not due to production but the problem with our binding proteins. Thyroid antibody tests are also available to help diagnose the cause of the thyroid problem. Antithyroid peroxidase or anti-TPO and anti-thyroglobulin antibodies or anti-TG in a patient with hypothyroidism result in a diagnosis of Hashimoto's Thyroiditis. The detection of thyroid stimulating autoantibodies to the thyroid stimulating hormone receptors, also called TSHR on the thyroid are used to help diagnose Graves' Disease.

#### **Andrea Ott-Vasconi:**

Graves' Disease and autoimmune disorder is one of the most common causes of hyperthyroidism and also one of the most difficult to diagnose. Which tests are recommended to aid in the diagnosis and management of Graves' Disease?

#### **Rea Castro:**

So, there are three different types of thyroid receptor antibodies: thyroid stimulating immunoglobulin, thyroid blocking, immunoglobulin, and neutral or cleavage antibodies. TSI or thyroid stimulating immunoglobulin is specific for Grave's Disease because it is the stimulating antibody that lead to hyperthyroidism. Therefore, the accurate analysis of TSI is key. So the 2016 American Thyroid Association Guidelines support the use of TSI testing as the first recommendation when suspecting hyperthyroidism. During treatment with an anti-thyroid drug, it is also recommended that TSI is used to monitor the efficacy. The level of TSI during therapy help manage the patient properly.

The ATA guidelines also recommend using TSI to identify and manage pregnancy patients, including postpartum follow-up. The 2018 European Thyroid Association Guideline for the management of Graves' Hyperthyroidism recommend the measurement of TSH-R-Ab as a sensitive and specific tool for rapid and accurate diagnosis and differential diagnosis of Graves' Disease. Differentiation of TSH-R-Ab functionality is helpful and predictive in Graves' patient during pregnancy and postpartum, as well as for extra thyroidal manifestations.

#### **Andrea Ott-Vasconi:**

And once diagnosed, it's also important to monitor a known condition. Which assays can be used for monitoring thyroid diseases?

#### **Rea Castro:**

TSH is used to monitor response to therapy. If a patient is prescribed a synthetic thyroxin to treat hypothyroidism, we need to monitor that response and adjust the dosage as needed. The American Association of Clinical Endocrinologists recommends 0.3 to 3.0 mIU per ml as the appropriate normal range for TSH, but endocrinologists often like to see the TSH level to be around one to 1.5. Another test, a thyroglobulin test, or Tg, is also available and is used to monitor thyroid cancer in patients who has had a thyroidectomy. A positive Tg test indicates that thyroid cells either normal or cancerous, are still present in our body.

After thyroidectomy, we expect the Tg level to be undetectable. Some people produce antithyroglobulin antibodies or anti-Tg. If you have anti-Tg imaging studies may be used to monitor for persistent or

recurrent disease. Lastly, for monitoring total T4, which is also used for hyperthyroid, can also be used for monitoring treatment when a patient is on an antithyroid drug.

**Andrea Ott-Vasconi:**

And what are the complications associated with thyroid disorders?

**Rea Castro:**

So since thyroid hormone affects nearly every tissue and organ system in the body, any disruption of the normal hypothalamic pituitary thyroid axis that affects TSH or T3 and T4 will manifest itself in really various ways, which is why getting accurate testing results as early as possible reduces the risk of mild disease becoming severe disease. So for example, in women, thyroid diseases can cause problems with a menstrual cycle such as causing irregular periods or even causing periods to stop for several months. So for women trying to get pregnant, the disruption thyroid disease can have on ovulation makes it even harder.

Also, cardiovascular diseases and thyroid dysfunction are closely interlinked. Both hyperthyroidism and hypothyroidism may cause alterations in cardiac function. Hyperthyroidism gives rise to palpitations, atrial fibrillation, systolic hypertension, heart failure, whereas hypothyroidism increases diastolic hypertension, pericardial effusion, and the risk of ischemic heart disease. Early recognition and treatment of thyroid dysfunction may therefore prevent adverse cardiovascular events in patients with or without preexisting cardiovascular disease.

It also impacts our kidneys. Serious hypothyroidism can lower the kidneys function often due to the decreased blood flow to the kidneys. Hypothyroidism can also lead to nervous system complication such as muscle weakness and nerve injury. Also, thyroid dysfunction affects bone health and it's linked to osteoporosis. Too much thyroid hormone increases the rate at which bone is lost. If the thyroxin level stays too high or the thyroid stimulating hormone level stays too low in your body for a long period of time, then there is a higher risk of developing osteoporosis.

**Andrea Ott-Vasconi:**

And hyper and hypothyroidism can affect pregnancy in several ways. What are some of the risks to the mother and to the baby?

**Rea Castro:**

So thyroid hormones are important in the normal development of the baby's brain and nervous system. Untreated hypothyroidism during pregnancy may truly adversely affect maternal and fetal outcomes and include miscarriage, preterm delivery, preeclampsia, low birth weight and stillbirth and impaired intellectual and psychomotor development of the baby. Hyperthyroidism in pregnancy is usually caused by Grave's Disease and this occurs in one to four of every 1000 pregnancies in the United States that actually may first appear in the patient during pregnancy. Untreated hyperthyroidism during pregnancy can lead to the same issues as hypothyroidism with the possibility of miscarriage, premature birth, low birth weight, and preeclampsia. Targeted screening for thyroid disease should be performed in pregnant women determined to be high risk, such as those with personal or family history of thyroid disease.

**Andrea Ott-Vasconi:**

Thank you Dr. Castro for this very insightful and informative discussion today on the important topic of thyroid disorders. I hope everyone enjoyed this podcast episode. Make sure to review sections within

the podcast description with suggested reading materials and links to learn more. Based on today's podcast, I'll leave you with our pop quiz. What complications can arise if thyroid disease is left undetected? You can go back and listen again if you'd like some more details.

Thank you so much for listening today. Please subscribe to QuidelOrtho's Science Bytes, our monthly podcast, brought to you by QuidelOrtho Corporation, where we are transforming the power of diagnostics into a healthier future for all. Take care.

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