

A new study found that 13 million Americans may be unaware of and undiagnosed for their thyroid conditions and that more widespread thyroid testing is needed. This number is double the previously suspected level of undiagnosed cases in the United States. The study was funded by thyroid drug Synthroid's manufacturer, Knoll Pharmaceutical Co.

The study, known as the Colorado Thyroid Disease Prevalence Study, set out to determine how common abnormal thyroid function actually is, and to look at the relationship between abnormal thyroid function, cholesterol levels, and thyroid symptoms. The researchers studied 25,862 participants at the Colorado statewide health fair in 1995. Among patients not taking thyroid medication, 8.9 percent were hypothyroid and 1.1 percent were hyperthyroid. This indicates 9.9 percent of the population had a thyroid abnormality that had most likely gone unrecognized. These figures suggest that nationally, there may be 13 million Americans with an undiagnosed thyroid condition.

The study also found that even a slight decrease in thyroid function -- what is sometimes referred to as "subclinical" or low-level hypothyroidism -- may raise cholesterol levels. These findings are consistent with what was reported on by the [American Association of Clinical Endocrinologists survey regarding cholesterol and thyroid disease in January of 2000](#). That study found that as many as ten percent of the 98 million Americans with high cholesterol levels may not know that their cholesterol is elevated due to undiagnosed thyroid problems.

The thyroid/heart disease/cholesterol linkage was further confirmed in the [February 15, 2000 Annals of Internal Medicine's publication of the Rotterdam Study results](#). The Rotterdam study found that older women with subclinical hypothyroidism were almost twice as likely as women without this condition to have blockages in the aorta, and were also twice as likely to have had heart attacks.

The thyroid is a butterfly-shaped gland that wraps around the windpipe, behind the "Adam's Apple" area of the neck. The hormones produced by the gland are essential to stimulating metabolism, growth, and the body's capacity to process calories. An underactive thyroid -- hypothyroidism -- affects more women than men, and the risk increases with age for both men and women. The symptoms of hypothyroidism include fatigue, depression, weight gain, hair loss, muscle and joint pains, and many other chronic and debilitating symptoms. Low thyroid can also be linked to increased levels of LDL -- "bad" cholesterol -- and risk of heart disease.

The Colorado Thyroid Disease Prevalence Study found, not surprisingly, that as thyroid function declined, patients reported more symptoms such as hoarse voice, constipation, feeling tired, puffy eyes, muscle cramps, slower thinking, among others. But there wasn't a clear-cut linkage between the proportion and type of symptoms reported, and the level of thyroid failure, and no one individual symptom was a clear indicator of thyroid failure.

The link between all stages of hypothyroidism and cardiovascular health, and the vague correlation between symptoms and disease state, points to the need for more widespread thyroid stimulating hormone (TSH) testing and more aggressive treatment, especially for subclinical patients.

Is This Revised Estimate of 13 Million Still Too Low?

While the Colorado Study has effectively doubled the estimated percentage of the population believed to be suffering from undiagnosed hypothyroidism, some doctors believe that relying on the TSH normal range as the only way to define hypothyroidism may mean that still more millions are hypothyroid, but undiagnosed and overlooked due to rigid interpretation of bloodtest results and a need to reevaluate the TSH normal range.

The key thing is of course that what doctors are always told is that TSH is the test that gives us a yes or no answer. And, in fact, I think that's fundamentally wrong. The pituitary TSH is controlled not just by how much T4 and T3 is in circulation, but T4 is getting converted to T3 at the pituitary level. Excess T3 generated at the pituitary level can falsely suppress TSH.

Many people may be suffering from minute imbalances that have not yet resulted in abnormal blood tests. If we included people with low-grade hypothyroidism whose blood tests are normal, the frequency of hypothyroidism would no doubt exceed 10 percent of the population. What is of special concern, though, is that many people whose test results are dismissed as normal could continue to have symptoms of an underactive thyroid. Their moods, emotions, and overall well-being are affected by this imbalance, yet they are not receiving the care they need to get to the root of their problems....Even if the TSH level is in the lower segment of the normal range, a person may still be suffering from low-grade hypothyroidism.

What are the Implications for the Public?

This study, the largest to date that has looked at the prevalence of thyroid disease, has some important implications for the public.

The estimated 10% of the population -- double the number previous thought -- that is suffering from undiagnosed hypothyroidism points to an urgent need for doctors to become better educated about and more proactive in testing for thyroid disease. Patients also need to become more informed, and insist on thyroid testing when doctors or HMO's are reluctant.

The researchers felt that a careful evaluation of patients' symptoms should be an important part in the diagnosis of hypothyroidism, and the existence of several symptoms in tandem should be a signal to test for thyroid problems. This is a change in focus, in which doctors have indicated that most patients would not even experience symptoms at subclinically hypothyroid TSH levels. It is hoped that this realization that the symptoms -- and negative health consequences such as higher cholesterol -- of subclinical hypothyroidism warrant that the warning symptoms be taken more seriously, and not dismissed in the catchall "stressed, depressed, PMS'd or pre-menopausal" non-diagnosis that many thyroid patients have for years before they are actually diagnosed.

Among patients taking thyroid medication, only 60% were within the normal range of TSH. The fact that forty percent of patients, a number that translates to millions of Americans, are already taking thyroid hormone and being treated by a doctor but are still not in TSH range is of great concern. Not only does this show the need for more frequent monitoring and adjustment of dosages -- versus the typical doctor's recommendation of maximum yearly testing -- but may in fact suggest that there are serious inadequacies in the current therapies, which primarily almost solely on synthetic thyroid hormone replacement known as levothyroxine (brandnames Synthroid, Levoxyl, Levothyroid, Eltroxin).

Dr. Donald Layman, Ph.D., is a professor of nutrition at the University of Illinois. He quotes that dieters receiving only 15% of their calories from protein have lower thyroid hormone levels but does not pay attention to the fact that they also have lower levels of thyroid binding globulin. He did not measure "Free T3" nor "Thyroid Binding Globulin". (See [Understanding Thyroid Lab Tests](#)) Dr. Layman's article was in reference to different diets and weight loss, and the data regarding thyroid hormone levels was reported only as an incidental finding. Somehow, the writers at Woman's World heard about this "incidental finding" in this article and

interviewed him. Dr. Layman realized that they were misinterpreting his data and said to them, "Any extrapolation of our data to thyroid would be inappropriate." He did not intend to link Tyrosine (as quoted), nor weight loss diets (which he studied) with the ability to regulate thyroid function. (Layman DK, et al. "A reduced ratio of dietary carbohydrate to protein improves body composition and blood lipid profiles during weight loss in adult women." J Nutr 2003; 133:411-417)

Dr. Glenn S. Rothfeld, M.D., has written many health books including "Thyroid Balance" (Amazon.com sales rank 5/20/03 14,719). This book is considerably less popular than three other books on thyroid ("Living Well With Hypothyroidism" by Mary Shomon (Amazon rank 5/20/03 -- 969), "Thyroid Solution" by Ridha Arem, M.D. (Amazon rank 5/20/03 -- 1,530), and "Thyroid Power" by Richard Shames, M.D. and Karilee Shames, R.N., Ph.D. (Amazon rank 5/20/03 1,848). It is not considered a key source for information regarding thyroid disease. He emphasizes tyrosine, the amino acid that is found in thyroid hormone. Although low levels of tyrosine have been associated with hypothyroidism, this is thought to be mainly due to low serum levels of iron, tetrahydrobiopterin, and NAD, all necessary for the conversion of the essential amino acid phenylalanine to tyrosine. Because it enhances intestinal absorption of iron, vitamin C can help restore tyrosine formation when there is a deficiency of iron. Iron deficiency is quite common in women and can be tested with a serum ferritin level.

Dr. Bruce Fife, N.D., no longer sees patients and now derives a majority (if not all) his income from the coconut oil industry. He has not published nor cited any research relating coconut oil to thyroid function. It is unclear whether he has IRB approval to safely conduct human studies. As he is not a MD or DO physician licensed to prescribe (or de-prescribe) prescription medication, his suggestion to "give up thyroid medications and simply use coconut oil instead," is improper. Inadequately treated hypothyroidism could lead to osteoporosis, early heart attacks, and other disability. Though foods are generally less toxic than refined prescription medications, they do have the potential for harmful effects if taken in excessive dosages. For example, too much consumption of Vitamin E in the form of d-alpha tocopherol prevents the absorption of beta- and gamma-tocopherols, increasing the risk for heart disease. Dr. Fife references a University of Colorado review article (not a research article) that speculates on the possibility that medium-chain triglycerides could preserve muscle glycogen during exercise. From this theorized discussion, it would be difficult to come to his conclusions that "coconut oil can increase your calorie-burning power by up to 50%," leading to a weight loss of "36 pounds a year without dieting."

Testing

“Unfortunately, they only did one type of test. Despite being called ‘ultra-sensitive,’ the ‘TSH’ blood test has its limitations. It isn’t accurate for everyone...”

- 1. Find out your thyroid test results from your doctor's office.**
- 2. If you can, get a hard copy printout for your own review and home medical files.**
- 3. If "normal" or "reference" ranges are not indicated on the lab results, ask your doctor's office to tell you what these ranges are.**
- 4. Note the level of your Thyroid Stimulating Hormone (TSH). At most labs in the U.S., up until late 2002, the normal range is from around 0.5 to 5.5. That range changed to .3 to 3 as of early 2003.**
- 5. If the TSH level is below normal, your doctor may determine that you are hyperthyroid (overactive thyroid.)**
- 6. If the TSH level is above normal, your doctor may determine that you are hypothyroid (underactive thyroid.)**
- 7. If your doctor ran a test called Total T4 or Total Thyroxine, normal range is approximately 4.5 to 12.5. If you had a low reading, and a high TSH, your doctor might consider that indicative of hypothyroidism.**
- 8. If your doctor ran a test called Total T4 or Total Thyroxine, normal range is approximately 4.5 to 12.5. If you had a low reading, and a low TSH, your doctor might look into a pituitary problem.**
- 9. If your doctor ran a test called Free T4, or Free Thyroxine, normal range is approximately 0.7 to 2.0. If your result was less than 0.7, your doctor might consider that indicative of hypothyroidism.**
- 10. If your doctor ran a test called Total T3, normal range is approximately 80 to 220. If your result was less than 80, your doctor might consider that indicative of hypothyroidism.**
- 11. If your doctor ran a test called Free T3, normal range is approximately 2.3 to 4.2. If your result was less than 2.3, your doctor might consider that indicative of hypothyroidism.**
- 12. If your test results come back "normal" but you have many of the symptoms or risk factors for thyroid disease, make sure you ask for an antibodies test. Some doctors believe in treating thyroid symptoms in the presence of elevated antibodies and normal TSH levels.**
- 13. If your test results come back "normal" but you have many of the symptoms or risk factors for thyroid disease, consider going to a reputable holistic M.D. or alternative physician for further interpretation and diagnosis.**

Tips:

1. **Laboratory reference ranges and normal ranges can differ from lab to lab. Always go by your lab's reference range and your doctor's diagnosis.**

Chronic thyroiditis (Hashimoto's disease)

Definition:

Chronic thyroiditis is an inflammation of the thyroid gland that frequently results in [hypothyroidism](#) (lowered thyroid function).

Alternative Names:

Hashimoto's thyroiditis; Struma lymphomatosa; Lymphadenoid goiter; Chronic lymphocytic thyroiditis; Autoimmune thyroiditis

Causes, incidence, and risk factors:

Chronic thyroiditis or Hashimoto's disease is a common [thyroid gland disorder](#) that can occur at any age, but it is most often seen in middle aged women. It is caused by a reaction of the immune system against the thyroid gland.

The onset of the disease is slow, and it may take months or even years for the condition to be detected. Chronic thyroiditis is most common in women and individuals with a family history of thyroid disease. It is estimated to affect between 0.1% and 5% of all adults in Western countries.

Hashimoto's disease may rarely be associated with other [endocrine](#) disorders caused by the immune system. When Hashimoto's disease occurs with adrenal insufficiency and type 1 diabetes mellitus, the condition is called type 2 polyglandular autoimmune syndrome (PGA II).

Less commonly, Hashimoto's disease occurs with hypoparathyroidism, adrenal insufficiency, and fungal infections of the mouth and nails in a condition called type 1 polyglandular autoimmune syndrome (PGA I).

Symptoms:

- [Intolerance to cold](#)
- [Weight gain](#) - mild
- [Fatigue](#)
- [Constipation](#)
- **Enlarged neck or presence of [goiter](#)**
- **Small or atrophic thyroid gland (late in the disease)**

- **Dry skin**
- **Hair loss**
- **Heavy and irregular menses**
- **Difficulty concentrating or thinking**

Additional symptoms that may be associated with this disease:

- [Weight gain \(unintentional\)](#)
- [Joint stiffness](#)
- [Facial swelling](#)

Note: There may be no symptoms.

Signs and tests:

Laboratory tests to determine thyroid function include:

- **Free [T4 test](#)**
- **[Serum TSH](#)**
- **[T3](#)**
- **Thyroid autoantibodies are frequently present:**
 - **antithyroid peroxidase antibody**
 - **[antithyroglobulin antibody](#)**

This disease may also alter the results of the following tests:

- **[Radioactive iodine uptake](#)**
- **Complete blood count**
- **Total cholesterol**
- **Serum sodium**
- **Serum prolactin**

Goiter

Definition:

A goiter is an enlargement of the thyroid gland that is NOT associated with inflammation or [cancer](#).

Causes, incidence, and risk factors:

There are different kinds of goiters. A simple goiter usually occurs when the thyroid gland is not able to produce enough thyroid hormone to meet the body's requirements. The thyroid gland compensates by enlarging, which usually overcomes mild deficiencies of thyroid hormone.

A simple goiter may be classified as either an [endemic](#) (colloid) goiter or a sporadic (nontoxic) goiter.

Endemic goiters occur within groups of people living in geographical areas with iodine-depleted soil, usually regions away from the sea coast. People in these communities might not get enough iodine in their diet. (Iodine is vital to the formation of thyroid hormone.) The modern use of iodized table salt in the U.S. prevents this deficiency; however, it is still common in central Asia and central Africa.

In most cases of sporadic goiter the cause is unknown. Occasionally, certain medications such as lithium or aminoglutethimide can cause a nontoxic goiter.

Hereditary factors may cause goiters. Risk factors for the development of a goiter include female sex, age over 40 years, inadequate dietary intake of iodine, residence in an endemic area, and a family history of goiter.

Symptoms:

- **thyroid enlargement varying from a single small [nodule](#) to massive enlargement (neck lump)**
- **[breathing difficulties](#), cough, or [wheezing](#) due to compression of the trachea**
- **[swallowing difficulties](#) due to compression of the esophagus**
- **neck vein distention and [dizziness](#) when the arms are raised above the head**

Signs and tests:

- **measurement of thyroid stimulating hormone (TSH) and thyroxine (T4) in the blood**
- **[thyroid scan](#) and uptake**
- **[ultrasound of thyroid](#) -- if nodules are present, a biopsy should be done to evaluate for thyroid cancer**

Hyperthyroidism

Definition:

Hyperthyroidism is an imbalance of [metabolism](#) caused by overproduction of thyroid hormone.

Alternative Names:

Thyrotoxicosis; Overactive thyroid

Causes, incidence, and risk factors:

The thyroid gland is located in the neck. It produces several hormones which control the way that every cell in the body uses energy ([metabolism](#)). The thyroid is part of the [endocrine](#) system.

Hyperthyroidism or thyrotoxicosis occurs when the thyroid releases too many of its hormones over a short ([acute](#)) or long (chronic) period of time. Many diseases and conditions can cause this problem.

These include [Graves' disease](#); non-cancerous growths of the thyroid gland or pituitary gland; tumors of the [testes](#) or ovaries; inflammation (irritation and swelling with presence of extra immune cells) of the thyroid due to viral infections or other causes; ingestion of excessive amounts of thyroid hormone; and ingestion of excessive iodine. Graves' disease accounts for 85% of all cases of hyperthyroidism.

Related topics:

- [Painless \(silent\) thyroiditis](#)
- [Factitious hyperthyroidism](#)
- [Hypothyroidism](#)
- [Graves' disease](#)

Symptoms:

- [Weight loss](#)
- [Increased appetite](#)
- **Nervousness**
- [Restlessness](#)
- [Heat intolerance](#)
- [Increased sweating](#)
- [Fatigue](#)
- [Frequent bowel movements](#)

- [Menstrual irregularities](#) in women
- [Goiter](#) (visibly enlarged thyroid) may be present

Additional symptoms that may be associated with this disease:

- [Weakness](#)
- [Sleeping difficulty](#)
- [Skin - clammy](#)
- [Skin blushing/flushing](#)
- [Pulse - bounding](#)
- [Nausea and vomiting](#)
- [Menstruation - absent](#)
- [Itching - overall](#)
- [Heartbeat sensations](#)
- [Hand tremor](#)
- [Hair loss](#)
- [Diarrhea](#)
- Breast development in men
- [Blood pressure - high](#)
- [Protruding eyes \(exophthalmos\)](#)

Signs and tests:

[Vital signs](#) (temperature, [pulse](#), rate of breathing, [blood pressure](#)) show increased [heart rate](#). Systolic blood pressure may be elevated. [Physical examination](#) may reveal thyroid enlargement or [goiter](#).

Laboratory tests that evaluate thyroid function:

- [Serum TSH](#) is usually decreased
- [T3](#) and free [T4](#) are usually elevated

This disease may also alter the results of the following tests:

- [Vitamin B-12](#)
- [TSI](#)

- [Triglycerides](#)
- [RT3U](#)
- [Radioactive iodine uptake](#)
- [Glucose test](#)
- [Cholesterol test](#)
- [Antithyroglobulin antibody](#)

Hypothyroidism

Definition:

Hypothyroidism is a condition in which the thyroid gland fails to produce enough thyroid hormone.

Alternative Names:

Myxedema; Adult hypothyroidism

Causes, incidence, and risk factors:

The thyroid gland, located in the front of the neck just below the larynx, secretes hormones that control [metabolism](#). These hormones are thyroxine (T4) and [triiodothyronine \(T3\)](#).

The secretion of T3 and T4 is controlled by the pituitary gland and the [hypothalamus](#), which is part of the brain. [Thyroid disorders](#) may result not only from defects in the thyroid gland itself, but also from abnormalities of the pituitary or hypothalamus.

Hypothyroidism, or underactivity of the thyroid gland, may cause a variety of symptoms and may affect all body functions. The body's normal rate of functioning slows, causing mental and physical sluggishness. The symptoms may vary from mild to severe, with the most severe form called myxedema, which is a medical emergency.

The most common cause of hypothyroidism is Hashimoto's thyroiditis, a disease of the thyroid gland where the body's immune system attacks the gland. Failure of the pituitary gland to secrete a hormone to stimulate the thyroid gland ([secondary hypothyroidism](#)) is a less common cause of hypothyroidism. Other causes include congenital defects, surgical removal of the thyroid gland, irradiation of the gland, or inflammatory conditions.

Risk factors include age over 50 years, female gender, [obesity](#), thyroid surgery, and exposure of the neck to [x-ray](#) or radiation treatments.

Symptoms:

Early symptoms:

- [weakness](#)
- [fatigue](#)
- [cold intolerance](#)
- [constipation](#)
- [weight gain \(unintentional\)](#)
- [depression](#)
- [joint or muscle pain](#)
- [thin, brittle fingernails](#)
- thin and brittle hair
- [pale](#) color

Late symptoms:

- **slow speech**
- [dry flaky skin](#)
- **thickening of the skin**
- [puffy face](#), hands and feet
- [decreased taste and smell](#)
- **thinning of eyebrows**
- [hoarseness](#)
- [abnormal menstrual periods](#)

Additional symptoms that may be associated with this disease:

- [overalls swelling](#)
- [muscle spasms \(cramps\)](#)
- [muscle pain](#)
- [muscle atrophy](#)
- [uncoordinated movement](#)
- [absent menstruation](#)
- [joint stiffness](#)

- [dry hair](#)
- [hair loss](#)
- [facial swelling](#)
- [drowsiness](#)
- appetite loss
- [ankle, feet, and leg swelling](#)
- [short stature](#)
- separated sutures
- delayed formation or absence of teeth

Signs and tests:

A [physical examination](#) reveals delayed relaxation of muscles during tests of reflexes. Pale, yellow skin; loss of the outer edge of the eyebrows; thin and brittle hair; coarse facial features; brittle nails; firm swelling of the arms and legs; and mental slowing may be noted. [Vital signs](#) may reveal slow [heart rate](#), [low blood pressure](#), and low temperature.

A [chest X-ray](#) may reveal an enlarged heart.

Laboratory tests to determine thyroid function include:

- [T4 test](#) (low)
- [serum TSH](#) (high in primary hypothyroidism, low or low-normal in secondary hypothyroidism)

Additional laboratory abnormalities may include:

- increased [cholesterol levels](#)
- increased liver enzymes
- increased serum [prolactin](#)
- low [serum sodium](#)
- a complete blood count ([CBC](#)) that shows [anemia](#)

• ***DISEASE:*** DEFECTS IN THRβ ARE A CAUSE OF THE SYNDROME OF GENERALIZED THYROID HORMONE RESISTANCE (GTHR), TRANSMITTED AS AN AUTOSOMAL DOMINANT TRAIT,

CHARACTERIZED BY GOITER, ABNORMAL MENTAL FUNCTIONS, INCREASED SUSCEPTIBILITY TO INFECTIONS, ABNORMAL GROWTH AND BONE MATURATION, TACHYCARDIA AND DEAFNESS. AFFECTED INDIVIDUALS MAY ALSO HAVE ATTENTION DEFICIT-HYPERACTIVITY DISORDERS (ADHD) AND LANGUAGE DIFFICULTIES. GTHR PATIENTS ALSO HAVE HIGH LEVELS OF CIRCULATING THYROID HORMONES (T3-T4), WITH NORMAL OR SLIGHTLY ELEVATED THYROID STIMULATING HORMONE (TSH)

Symptoms of Untreated Hypothyroidism in Adults

- **Cardiovascular System (slowed heart rate, increased diastolic blood pressure)**
- **Central Nervous System (decreased concentration, loss of interest and/or pleasure, depression)**
- **Gastrointestinal Tract (decreased secretion of digestive juices, constipation)**
- **Musculoskeletal System (muscle stiffness, cramps, weakness, pain, muscle stretch reflexes, muscle enlargement, atrophy, joint pain and stiffness)**
- **Kidneys (fluid retention and edema)**
- **Liver (increased LDL cholesterol in the blood, elevated triglycerides in the blood)**
- **Reproductive System (abnormally heavy menstrual bleeding, missed ovulation, decreased fertility, missed menstrual periods)**
- **Skin and Hair (thickening and dryness of the skin, dry, coarse hair and/or loss of hair, loss of lateral eyebrow hair)**

Symptoms of Untreated Hyperthyroidism in Adults

- **Cardiovascular System (increased heart rate, increased diastolic blood pressure, heart flutter - atrial fibrillation)**
- **Central Nervous System (difficulty sleeping, difficulty concentrating, nervousness, irritability, changes in vision)**
- **Gastrointestinal Tract (increased frequency of bowel movements, increased appetite, weight loss)**
- **Musculoskeletal System (fatigue and muscle weakness)**

- Kidneys (leg edema)
- Reproductive System (decreased menstrual flow, reduced fertility)
- Endocrine System (enlarged thyroid)
- Other (intolerance to heat, increased sweating, enlargement and protruding of the eyes)

Etiology

The causes of subclinical hyperthyroidism are similar to those that cause overt thyrotoxicosis². (Table 1). In iodine-sufficient regions such as the United States, overt hyperthyroidism in women of all ages is most commonly due to Graves' disease, and early Graves' disease may present as subclinical hyperthyroidism. Multinodular or uninodular toxic goiter is another major cause of subclinical hyperthyroidism, especially in areas of marginal iodine intake. The natural history of multinodular goiter (Plummers's disease) appears to be the gradual development of autonomy, leading first to subclinical and then to overt hyperthyroidism³. The prevalence of thyroid nodularity generally increases with age, especially in women. In one English post-mortem study 23 % of women over age 60 had nodular glands⁴. A German post-Merck mortem study (in an area of moderate iodine deficiency) found nodules in 88 % of elderly women⁵.

Graves' disease
Toxic adenoma
Toxic multinodular goiter
Silent thyroiditis
Subacute thyroiditis
Exogenous thyroid hormone
Iodine and iodine-containing drugs and radiographic contrast agents

Subclinical thyrotoxicosis is frequently iatrogenic, the result of overzealous thyroid hormone replacement therapy for hypothyroidism, or of TSH suppressive therapy for thyroid cancer. In older patients with autonomous nodules, hyperthyroidism may be precipitated by an exogenous iodine load due to radiocontrast agents, amiodarone, and other iodine-containing medications,

including all forms of kelp.

Subclinical hyperthyroidism must be differentiated from other causes of low serum TSH values including non-thyroidal illness, pregnancy, pituitary or hypothalamic insufficiency, and the use of medications including glucocorticoids, dopamine, aspirin, furosemide, and fenclofenac ⁶. A suppressed TSH may be a transient finding. For example, in the Framingham Heart Study, 88 % of those who had subclinical hyperthyroidism at baseline had serum TSH values > 0.1 on repeat testing four years later ⁷

The Thyroid and Down Syndrome

by Len Leshin, MD, FAAP

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Normal Function

The thyroid gland sits at the base of the front of the neck and makes thyroid hormone from iodide, thyroglobulin and tyrosine. This results in the production of thyroxine (T4), which is a "prohormone" (it's inactive but just one step away from becoming a real hormone), and the actual thyroid hormone, T3. Both T3 and T4 are secreted by the thyroid into the blood stream. T4 is converted to T3 by the thyroid, kidneys, and liver. And it's the T3 that's so important for normal growth and development of infants and children, and normal metabolism of all ages.

So where does the Growth Hormone (GH) fit in? The GH, synthesized in the part of the brain called the pituitary, appears to be the mediator between the thyroid hormone and the individual tissues. You can also include somatomedins, a group of proteins under the control of GH, as mediators between T3 and body tissues.

Thyroid function is controlled by Thyroid Stimulating Hormone (TSH), a hormone made in the hypothalamus and pituitary. If the brain detects that T3 levels are low, more TSH is made which tells the thyroid to make more T4 and T3. If levels are too high, the brain slows down making TSH.

Hypothyroidism

This is the state of not making enough thyroid hormone, and is the most common thyroid problem associated with DS. This can be present at birth (congenital) or may occur at any age (acquired). Every state in the US and many other countries routine screen all newborns for hypothyroidism. In newborns and infants with DS, the most common reason for hypothyroidism is that the thyroid did not form correctly in the fetus. In acquired hypothyroidism, the most common reasons in toddlers and older children with DS is (1) autoimmunity (where the body makes antibodies against its own thyroid) and (2) thyroiditis, where the thyroid tissue becomes replaced with white blood cells and fibrous tissue (Hashimoto thyroiditis).

The symptoms of low thyroid hormone are difficult to pick up, especially in infants. They include decreased growth, decreased development, an enlarged tongue, decreased muscle tone, dry skin and constipation -- all of which might be expected in an infant with DS. So, it is recommended that all infants with DS be checked at birth, 6 months of age, 1 year of age, and once a year thereafter for thyroid function, regardless of their growth.

Screening for thyroid function in infants usually involves only a TSH level; if the TSH is elevated, then the T4 will be checked. In older infants and children, a T4 and TSH is recommended, and some doctors include a measurement of T3 as well. Typically in hypothyroidism, the T4 will be low and the TSH will be elevated (as the brain is trying to tell the thyroid to get going).

Some infants and young children have blood tests that show a normal T4 but a high TSH. This condition is called "idiopathic hyperthyrotropinemia." While the cause isn't clear, this may reflect a regulatory defect of TSH, or it may be a sign of impending true hypothyroidism. Some endocrinologists will recommend retesting in 3 to 6 months, and others will recommend treating as if it were an early hypothyroid state.

Treatment is the replacement of thyroid hormone with synthetic thyroxine. The dose is managed by watching sequential blood tests to see how the thyroid responds. Treatment is usually needed for life. It should be noted that if the parents have become used to a calm, sedate child who is hypothyroid, the replacement will look as if the child has suddenly become hyperactive, when in fact the child is returning to his or her "natural" state.

Since T3 is the active hormone and the body converts T4 (thyroxine) to T3, many people have wondered why we supplement with T4 instead of T3. In fact, there was a medication called Armour thyroid that used to be used; this was made from ground up beef thyroids. The problem was that since it was a beef protein, it tended to provoke antibodies against it, and eventually stopped working for the patient. The reason we use synthetic T4 instead of developing synthetic T3 is that (1) it's pretty rare to have any problems converting T4 to T3, and (2) the body stores thyroid hormone as T4, so giving T4 builds up the natural reserve capacity of the body.

Hyperthyroidism

While not anywhere near as common as hypothyroidism, this condition does occur. The usual cause is, again, autoimmune disease, but in hyperthyroidism, the immune system cranks up the thyroid. (This is called *Graves Disease*.) Symptoms include rapid

heart rate, nervousness, sweating, decreased attention span, flushed skin, always feeling hot and loss of hair. Often these children will have a noticeably enlarged thyroid.

Testing here includes TSH (low), T3 (elevated) and T4 (elevated).

There are three possible treatments of hyperthyroidism. One treatment is aimed at blocking the action of the thyroid hormone on body tissues. This involves the use of antithyroid drugs, and are often the first treatment used. However, almost all of these drugs can cause significant side effects. A second treatment is surgery to remove part or all of the thyroid; and then the child or adult is begun on thyroid replacement if needed. The third treatment is the use of radioactive iodide, which destroys the thyroid's ability to produce thyroid hormone. The patient then takes replacement thyroid hormone. However, radioactive iodide is not often used in children because of the risk of thyroid carcinoma.

At the present time, there is no clear consensus on the best way to treat hyperthyroidism in children with DS.

Thyroid, DS and Controversy

Before the genetic reason of Down Syndrome was known, many people thought that DS was caused by hypothyroidism. In 1896, 20 years after Langdon Down first described "mongoloids," Telford Smith reported that giving thyroid therapy improved physical and mental conditions of these children. For decades later, researchers argued if all children with DS had hypothyroidism or not. With improved lab tests, the true picture emerged of most children with Down syndrome having normal thyroids.

There have been many claims for giving all children with DS thyroid hormone replacement, regardless of their blood tests. Dr. Turkel included thyroid hormone in his "U" series, Harrell's paper in 1981 on vitamin and mineral replacement included thyroid hormone therapy, and one researcher, Clemens Benda, advocated giving all children with DS a mixture of thyroid and pituitary gland. However, there is no known benefit from giving thyroid hormone to children with DS who have normal thyroid function, and could be detrimental.

Some researchers have claimed that there is a "low-borderline" thyroid state, and the thyroid tests could be normal as the body is able to partially compensate. However, research shows that giving thyroid replacement to individuals with DS and low-normal thyroid tests had no cognitive improvement.

Other people have latched on to a condition called Wilson's syndrome, called after the Dr. Wilson who first described it. Dr. Wilson believes that thyroid disease can be present with normal blood test, and evidenced by a low blood temperature and a collection of signs and symptoms, and then treated with a special thyroid replacement product. This has little to do with Down syndrome, except that some people have recently come forward claiming that hypothyroidism in people with DS may not be picked up with routine blood tests. In reality, there is no scientific evidence supporting these claims. For more information on this topic, see the [American Thyroid Association's statement on Wilson's syndrome](#).

Summary of Results --- 18 Human Thyroid PCB Studies

(each entry represents a finding in a study --- some studies had multiple findings)

Keep in mind that not all studies are equal in size or quality. Some examine the effects of old PCB commercial mixtures (which had variable composition), or just one or two individual types of PCBs (out of 209 possible.) Some of the studies are from the 1970s when scientists were just learning about thyroid effects. Some studies use high and some use low doses of PCBs. In some cases, the exact PCB dose was unknown. The types of PCBs which have lingered in our area and accumulated in Fox River and Green Bay fish are likely to be the more toxic and persistent PCB types (which are most similar to thyroid hormones.)

- **PCB exposure during adulthood was associated with impairments in memory and learning**
- **executive and visual-spatial function were unaffected**
- **PCBs and dioxins as found in the normal population have an effect on thyroid metabolism in humans.**
- **TT3 and TT4 levels decreased with increasing levels of PCBs and dioxin**
- **TSH levels were significantly elevated in newborns with higher PCB and dioxin levels**
- **decrease in TT4 and FT4 levels in human infants**
- **increase in TSH levels**
- **psychomotor development was negatively influenced**
- **increasing PCB and dioxin doses correlate with decreasing thyroid hormones in mothers' milk and blood plasma**
- **increasing dioxin exposure correlates with higher thyroid stimulating hormone (TSH) in newborn infants**
- **background levels of PCBs are only slightly related to serum concentration of total thyroxine, free thyroxine, and thyroid stimulating hormone at birth**

- dioxin linked to increased total thyroxine (tT4) --- (certain PCBs are dioxin-like)
- dioxin linked to increased thyroxine-binding globulin
- dioxin linked to increased thyrotropin (TSH)
- increased dioxins (& related compounds) correlate with reduced thyroxine (T4) levels (certain PCBs are dioxin-like)
- slight alteration of the thyroid metabolism (still within normal limits) after increased exposure to dioxides and PCB
- no grounds to advise against breast feeding
- no impaired thyroid function, as revealed by plasma levels of TSH and thyroxine
- serum triiodothyronine (T3) and thyroxine (T4) levels were significantly higher
- hyperthyroxinemia
- T4 ratio was significantly higher
- thyroglobulin antibody in Yusho patients is not frequent and it may be associated with blood PCB concentration
- 8.6% had elevated TSH levels
- increased levels of PCBs, dioxins and furans in breastmilk correlated with decreased thyroxine (T4) and triiodothyronine (T3)
- background levels of PCBs, dioxins and furans may affect thyroid hormone status in infants
- enlarged thyroids
- no relation between PCB and thyroid hormone or creatine kinase and thyroid hormone was observed
- significant differences in thyroxine (T4) and T4-RT3 index, correlated with PCB exposure
- thyroid function was normal.
- thyroid changes occurred, consistent with PCB exposure
- more research is needed, to include thyroid status

Summaries of 40 Study Reviews

(each entry represents a finding in a study --- some studies had multiple findings)

- **altered thyroid hormones have been consistently seen in human populations at background levels of PCB exposure**
- **PCBs bear a striking structural resemblance to thyroid hormones**
- **PCBs act as agonists, antagonists, and partial agonists to thyroid hormones (ie: PCBs interfere)**
- **inappropriate levels of thyroid hormones at key moments can produce permanent brain damage**
- **PCBs and dioxins are structurally similar to thyroid hormones**
- **PCBs and dioxins have binding characteristics similar to thyroid hormones**
- **PCBs and dioxins can either decrease or mimic the biological action of thyroid hormones**
- **deficient or excessive thyroid hormones can cause irreversible neurological damage in the womb or infancy**
- **mothers or children with existing thyroid disorders could experience greater harm even at low PCB levels which leave other people unharmed**
- **PCB exposed adults with existing thyroid disorders may face greater risk of developing brain, motor, or metabolic dysfunction**
- **evidence is increasing that PCBs impair learning, memory and attentional processes in children**
- **such neurodevelopmental effects may be linked to alterations in hormone binding to the thyroid hormone receptor**
- **thyroid hormones are essential for normal behavioral, intellectual, and neurological development**
- **PCBs alter serum thyroid hormone levels in humans**
- **hydroxylated PCBs (metabolized in the body) compete with thyroid hormones for binding sites**
- **PCBs and dioxins can alter human thyroid hormone status**
- **thyroid hormone alterations have been observed in mothers and infants exposed to background levels of PCBs**

- thyroid hormones stimulate development of the central nervous system in embryos
- the thyroid system is linked to other important body systems that use similar biochemical signals
- PHAHs [which include PCBs] can disrupt the thyroid hormone system at a multitude of interaction sites, which may have a profound impact on normal brain development
- adverse effects may occur within the range of current background human body levels of PCBs in the general population
- use of the dioxin Toxic Equivalency Factor (TEF) may underestimate risk of neurodevelopmental effects
- hyper- and hypothyroidism can be caused by PCBs and dioxins
- the hypothalamic-pituitary-ovarian-axis can be damaged directly by contaminants, but also indirectly through changes in thyroid hormone secretion.
- thyroid effects can be highly relevant to prenatal and postnatal development
- Toxic Equivalency Factors (TEFs) are inappropriate for estimating PCB thyroid effects
- only certain types of PCBs affect thyroid hormone levels
- PCBs in concentrations commonly found in humans can induce significant increases in the levels of free thyroxine in the serum by competing with the thyroid hormone binding proteins present in the serum --- leading to hypothyroidism
- PCB commercial mixtures (Aroclors) have been shown to produce thyroid alterations
- even low doses of PCBs interact with the thyroid system
- dioxins are linked to subcutaneous sarcomas and tumors of the thyroid (cancer) --- (certain PCBs are dioxin-like)
- PCBs exhibit hormonal activity and bind transthyretin, a thyroid hormone binding protein
- PCBs are thyroid disrupting
- PBBs (polybrominated biphenyls) may also affect thyroid hormone status

- hydroxylation (metabolic conversion) of PCBs or PBBs may play an important role
- hydroxylated PCBs (metabolized) are potent inhibitors of T2 (diiodothyronine) and probably T3 (triiodothyronine)
- inhibition of T3 (a thyroid hormone) may cause developmental neurotoxicity (brain damage)
- two models indicate a structural relationship between some PCBs and thyroid hormones
- PCBs are reactive with thyroxine (T4)
- PCBs are accumulated in the thyroid gland
- hydroxylated PCBs may decrease thyroid hormone levels
- 60% of 65 other industrial chemicals (mostly pesticides) also interfered with thyroid hormones (therefore, humans face combined impacts)
- subclinical effects may be present in the background population of humans
- organochlorine compounds (such as PCBs) are associated with abnormal thyroid function
- PCBs, dioxins and furans are associated with disease of the thyroid
- thyroid hormones may play a role in oxidative DNA damage which leads to cancer
- PCBs are implicated in tumor (cancer) induction as an indirect result of oxidative DNA damage
- common food poisoning symptoms include thyroid function changes
- dioxin in breast milk may affect infants' thyroid function
- more studies of thyroid functionality are needed, because human exposure to PCBs is inevitable
- alterations in neurotransmitter systems and thyroid function may underlie behavioral dysfunction
- hexachlorobenzene correlates with thyroid cancer ---
[hexachlorobenzene is closely related to certain PCBs]
- PCBs and dioxins reduce circulating thyroid hormone levels
- PCBs cause blood-level alterations and affect the circadian rhythm

- thyroid function is detrimentally impacted by chemical exposures
- thyroid function is adversely affected by certain man-made chemicals
- PCBs have known or suspected adverse effects on the human thyroid
- need to investigate the potential harm posed by these factors in the quantities commonly encountered
- more research is needed
- new legislation requires EPA to test chemicals for anti-thyroid activities and effects on steroid/thyroid hormone synthesis

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Human Thyroid PCB Studies

This is not a complete list of all studies on this topic. For more studies, visit the [TOXNET](#) database operated by the National Library of Medicine (the source of these abstracts).

Study #1

- PCB exposure during adulthood was associated with impairments in memory and learning
- executive and visual-spatial function were unaffected

An association between in utero polychlorinated biphenyl (PCB) exposure and impaired childhood intellectual functioning has been reported, but the potential impact of PCB exposure during adulthood on intellectual functioning has received little attention. We assessed the impact of PCBs and other fish-borne contaminants on intellectual functioning in older adults. The subjects were 49- to 86-year-old Michigan residents recruited from an existing cohort. Fish eaters ate > 24 lb of sport-caught Lake Michigan fish per year and non-fish eaters ate < 6 lb of Lake Michigan fish per year. A battery of cognitive tests including tests of memory and learning, executive function, and visual-spatial function was administered to 180 subjects (101 fish eaters and 79 non-fish eaters). Blood samples were analyzed for PCBs and 10 other contaminants. We evaluated cognitive outcomes using multiple regression. PCBs and dichlorodiphenyl dichloroethene (DDE) were markedly elevated in fish eaters. After controlling for potential confounders PCB, but not DDE, exposure was associated with lower scores on several measures of memory and learning. **These included the Weschler Memory Scale verbal delayed recall ($p = 0.001$), the semantic cluster ratio ($p = 0.006$), and list A,**

trial 1 ($p = 0.037$), from the California Verbal Learning Test. In contrast, executive and visual-spatial function were not impaired by exposure to either PCBs or DDE. In conclusion, PCB exposure during adulthood was associated with impairments in memory and learning, whereas executive and visual-spatial function were unaffected. These results are consistent with previous research showing an association between in utero PCB exposure and impairments of memory during infancy and childhood. (Schantz et al, 2001)

Study #2

- PCBs and dioxins as found in the normal population have an effect on thyroid metabolism in humans.
- TT3 and TT4 levels decreased with increasing levels of PCBs and dioxin
- TSH levels were significantly elevated in newborns with higher PCB and dioxin levels
- mothers and 418 children studied

Dioxins and polychlorinated biphenyls (PCBs) are potentially hazardous compounds that can alter the thyroid hormone homeostasis as shown in animal studies. We investigated thyroid hormone levels in women around delivery and in their infants just after delivery, at 2 wks and 3 months of age. Dioxin and PCB levels were measured in human milk and in maternal and umbilical cord plasma. (Table: see text). **Conclusions:** 1) TT3 and TT4 levels are negatively correlated to PCB and dioxin levels as can be found in the Dutch population. 2) TSH levels in newborns are significantly elevated at higher PCB and dioxin exposure. 3) These results indicate that PCBs and dioxins as found in the normal population have an effect on thyroid metabolism in humans. (Koopman-Esseboom et al, 1994)

Study #3

- decrease in TT4 and FT4 levels in human infants
- increase in TSH levels
- psychomotor development was negatively influenced
- mothers and 418 children studied

A prospective longitudinal follow-up study assessing neurodevelopment (according to Prechtl) was done in a cohort of 418 Dutch Caucasian full-term infants in the second week after birth and at 18 months of age. PCB levels were measured in maternal plasma in the last month of pregnancy and in umbilical cordblood. Dioxins were measured in breastmilk and formula samples. Half of the infants were breast-fed, the other half formula-

fed. In the second week after birth, exposure to higher levels of PCBs and dioxins was related to reduced neonatal neurological optimality scores and to a higher incidence of hypotonia. At 18 months of age higher transplacental exposure to PCBs was related to reduced neonatal neurological optimality scores. There was no relation with clinical relevant neurological abnormalities. In the Rotterdam cohort, thyroid hormone levels were measured. Higher exposure to PCBs and dioxins was related to a decrease in TT4 and FT4 levels and an increase in TSH levels in the infants. **Mental development was not negatively influenced. However, psychomotor development was negatively influenced by a higher exposure to PCBs and dioxins. (Koopman-Esseboom et al, 1995)**

Study #4

- **increasing PCB and dioxin doses correlate with decreasing thyroid hormones in mothers' milk and blood plasma**
- **increasing dioxin exposure correlates with higher thyroid stimulating hormone (TSH) in newborn infants**
- **studied 400 mother-infant pairs**

Polychlorinated biphenyls (PCBs) and dioxins are potentially toxic compounds which occur widely in the environment. Their effects on the growth and development of infants at the levels currently found in highly industrialised western countries is not well known. This Dutch multicenter study, combining animal and human studies, tries to answer this question. Animal studies showed that PCB 169, given once during pregnancy at a dose of 1.8 g kg⁻¹ bodyweight, has an effect on developmental parameters, dopamine regulation and fertility. Effects on thyroid hormones were also found in animals, probably due to both a competitive binding of PCB metabolites to the thyroxine binding protein and increased glucuronidation. Perhaps to compensate for this, an increased diiodase activity in the brain was found. Human studies involved 400 mother-infant pairs, half of them being breast-fed, the other half were fed a formula devoid of PCBs and dioxins. PCB levels were measured in serum and dioxin and PCB levels in breastmilk. Levels were found to be as high as previously found in highly industrialised countries. Growth and development were carefully documented, but no data are as yet available. In pregnant women, a significant negative correlation was found between some dioxin and PCB congeners in milk and plasma thyroid hormones, while newborn infants showed higher thyroid stimulating hormone (TSH) at higher levels of dioxin exposure. In summary, data from this combined multicenter study involving animals and humans increases our insight into the potentially negative effects of PCBs and dioxins on growth and development. (Sauer et al, 1994)

Study #5

- background levels of PCBs are only slightly related to serum concentration of total thyroxine, free thyroxine, and thyroid stimulating hormone at birth
- studied 160 children

Polychlorinated biphenyls (PCBs) are industrially produced environmentally persistent compounds. In developed countries all humans have detectable levels in blood and other tissues. PCBs alter thyroid hormone metabolism in animal experiments, and human data suggest background-level exposure may have similar effects in neonates. We evaluated this possible effect among 160 North Carolina children whose in utero PCB exposure was estimated on the basis of the mother's PCB levels in milk and blood, in 1978-1982 (estimated median PCB level in milk at birth, 1.8 mg/kg lipid). Their umbilical cord sera were thawed in 1998 and assayed for total thyroxine, free thyroxine, and thyroid stimulating hormone. We found that PCB exposure was not strongly related to any of the thyroid measures. For example, for a one unit change in milk PCB concentration (mg/kg lipid), the associated multivariate-adjusted increase in thyroid stimulating hormone level was 7% (95% confidence limits (CL) = -6, 21). Despite the possibility of sample degradation, these data suggest that within the range of background-level exposure in the United States, in utero PCB exposure is only slightly related to serum concentration of total thyroxine, free thyroxine, and thyroid stimulating hormone at birth. (Longnecker et al, 2000)

Study #6

- dioxin linked to increased total thyroxine (tT4) --- (certain PCBs are dioxin-like)
- dioxin linked to increased thyroxine-binding globulin
- dioxin linked to increased thyrotropin (TSH)
- studied 38 infants

Animal studies have shown that dioxins influence plasma thyroid hormone concentrations. To investigate the effect of chlorinated dioxins and furans on thyroid hormone concentrations in humans, we studied 38 healthy breast-fed infants. The study population was divided into two groups according to the dioxin concentrations in milk fat of their mothers. Blood samples were taken at birth and at the ages of 1 and 11 weeks. At birth a tendency to higher total thyroxine (tT4) concentrations was found in the high exposure group. At the ages of 1 and 11 weeks the increase of mean tT4 concentrations and tT4/thyroxine-binding globulin ratios in the high exposure group reached significance as compared to the low exposure group. At birth and 1 week after birth, mean thyrotropin (TSH) concentrations were similar in both groups, but at the age of 11 weeks the

mean TSH concentrations were significantly higher in the high exposure group. We postulate that the observed plasma tT4 elevation in infants exposed to dioxins before and after birth is the result of an effect on the thyroid hormone regulatory system. (Pluim et al, 1993)

Study #7

- increased dioxins (& related compounds) correlate with reduced thyroxine (T4) levels (certain PCBs are dioxin-like)
- mothers and 36 children studied

We investigated PCDDs and related compounds in the blood of young Japanese women, approximately 20 years of age, who had not yet had children, and discussed how the TEQ level of PCDDs and related compounds in their blood may affect the next generation. Means of total TEQ levels were 0.063 pg/g for whole blood basis and 21 pg/g for lipid basis. TEQ of PCDDs, PCDFs and coplanar PCBs accounted for about 43, 34 and 23% of the total TEQ in the whole blood basis, respectively. In the lipid basis, their values were about 44, 34 and 22%, respectively. Previously, we investigated PCDDs and related compounds levels in mother's breast milk, lymphocyte subpopulation and thyroid function of their children, and found negative correlations between the TEQ level of PCDDs and related compounds and CD4+/CD8+, and/or the TEQ level of PCDDs and related compounds and the T4 level in 36 mothers and children. Of these cases, the average age was approximately 28 years. PCDDs and related compounds may be related to immunopathy, such as atopic dermatitis. The effects of PCDDs and related compounds on babies of young Japanese women are important and must be further evaluated. (Iida et al, 1999)

Study #8

- slight alteration of the thyroid metabolism (still within normal limits) after increased exposure to dioxides and PCB
- no grounds to advise against breast feeding

As a part of the SGO Health Research Promotion Programme, in collaboration with the Toxicological Research Stimulation Programme, a research programme in the field of toxicology was realized. The study ran from 1990 to 1994 (4 years) and comprised animal and clinical research into the possible adverse effects of exposure of the foetus and the neonate to polychlorobiphenyls (PCBs), polychlorodibenzoparadioxins and polychlorodibenzofurans via the placenta and maternal milk. The clinical studies in neonates revealed a slight alteration of the thyroid metabolism (still within normal limits) after increased exposure to dioxides and PCB (as measured in maternal plasma, cord plasma and maternal milk), while slight neurological abnormalities without clinical relevance were also observed. It

is concluded from these study results that there are no grounds to advise against breast feeding. (Petit, 1997)

Study #9

- no impaired thyroid function, as revealed by plasma levels of TSH and thyroxine
- studied 12 hospitalized children

It has been shown by others that offspring of mothers who had been exposed to dioxins and polychlorinated biphenyls (PCBs) during pregnancy have elevated plasma levels of thyroid-stimulating hormone (TSH) for at least 3 months after birth and reduced plasma levels of free and total thyroxine during the second week after birth. As elevated levels of dioxins and PCBs can thus alter thyroid hormone status, the relation between the levels of some polychlorinated organic compounds in the blood lipids and growth and thyroid hormone status was studied in 12 hospitalized schoolchildren from the Aral Sea region known to have high exposure to such compounds. Their level of PCBs was two to four times higher than in healthy Stockholm children. Their height was found to be lower than in healthy Swedish children of the same age mean (SDS -0.52) and the body mass index (BMI) was inversely correlated to the total concentrations of PCBs and dichlorodiphenyltrichloroethane (DDT) and its metabolite dichlorophenyldichloroethylene (DDE) in the blood lipids. As the levels of insulin-like growth factor- were reduced to the same extent as the BMI it seems likely that PCBs and DDT cause malnutrition as a result of malabsorption. None of the children had any impairment of thyroid function, as revealed by the plasma levels of TSH and thyroxine. **Although the concentrations of beta-hexachlorocyclohexane (beta-HCH) and DDE were extremely high in some of the children there was no relation between thyroid hormone status and the blood lipid levels of PCBs, hexachlorocyclohexane and DDT. However, the concentration of dioxins was not analysed. (Mazhitova et al, 1998)**

Study #10

- serum triiodothyronine (T3) and thyroxine (T4) levels were significantly higher
- hyperthyroxinemia
- T4 ratio was significantly higher
- studied 123 poisoning victims 16 years later

Thyroid function was investigated in 123 yusho patients who were exposed to toxic levels of polychlorinated biphenyls (PCBs) 16 years ago. In yusho patients, compared with the patients without evidence of yusho or normal controls, the serum triiodothyronine (T3) and thyroxine (T4) levels were

significantly higher, while thyroid stimulating hormone (TSH) levels measured by sensitive assay were normal. There was no difference in serum levels of albumin, alkaline phosphatase, total cholesterol, and thyroxine binding globulin (TBG) between the two groups and the prevalence of positive antithyroid autoantibodies was almost the same, suggesting that hyperthyroxinemia in yusho patients was not due to increased TBG binding or abnormal autoimmune mechanism. Serum free T4 levels, however, were not elevated, although T4 ratio was significantly higher. The thyroid hormone levels were higher than normal value in 4 of 123 yusho patients but only 1 case had clinical symptoms such as excessive perspiration. Despite (incomplete abstract) (Murai et al, 1987)

Study #11

- thyroglobulin antibody in Yusho patients is not frequent and it may be associated with blood PCB concentration
- 8.6% had elevated TSH levels
- studied 81 patients, 28 years after accidental PCB poisoning

To evaluate chronic effect of polychlorinated biphenyl (PCB) on thyroid functions, thyroid hormone levels and thyroidal autoantibodies were studied in 81 patients with Yusho in 1996. Serum level of thyroid stimulating hormone (TSH) was elevated in 7 cases (8.6%). All of them showed normal triiodothyronine (T3), thyroxine (T4) and free T4 levels, and regarded as latent hypothyroidism. There were no significant correlations between blood PCB concentrations and TSH levels, T2 levels, T4 levels or free T4 levels. Thyroglobulin antibodies were detected in 8 cases (19.5%) of 41 Yusho patients with high PCB concentration (higher than 3.0 ppb), and in only one case (2.5%) of 40 patients with low PCB concentration (lower than 2.9 ppb). We conclude that thyroglobulin antibody in patients with Yusho is not frequent and it may be associated with blood PCB concentration. (Tsuji et al, 1997)

Study #12

- increased levels of PCBs, dioxins and furans in breastmilk correlated with decreased thyroxine (T4) and triiodothyronine (T3)
- background levels of PCBs, dioxins and furans may effect thyroid hormone status in infants
- studied 36 breast-fed infants

Effects of postnatal exposure to polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar polychlorinated biphenyls (Co-PCBs) on thyroid hormone status were studied in the peripheral blood of 36 breast-fed Japanese infants. Estimated total intakes of these chemicals in toxic equivalent quantity (TEQ) converted

into 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) from the breast milk significantly and negatively correlated with the levels of triiodothyronine (T3) and thyroxine (T4) in the blood of breast-fed babies. Therefore, exposure to background levels of the highly toxic organochlorine chemicals through the breast milk may cause some effects on thyroid hormone status in Japanese infants. (Nagayama et al, 1998)

Study #13

- enlarged thyroids
- abstract incomplete --- more effects may have been noted
- studied 372 women

This review presents the definition of main groups of organic chlorinated pollutants (polychlorinated biphenyls, dibenzodioxines, dibenzofurans, hexachlorobenzene, hexachlorocyclohexane, DDT etc.). Moreover, the similarity of their effects with those of steroid and thyroid hormones either via steroid/thyroid receptor or via specific Ah-receptor is described. Special attention is paid to their effects on the thyroid gland in experimental conditions as well as on professionally and nonprofessionally exposed population. Finally, own preliminary data are presented which were obtained by the examination of 249 employees of the factory Chemko producing polychlorinated biphenyls in 1955-85 as compared with control groups of 218 adults from Moldava, Trebišov and Košice and 278 women from Orava. In women from Chemko the frequency of thyroid volumes (by ultrasound) over 22,1 ml was 40/202, while that from Moldava was 16/170 ($p < 0.001$). In the employees of Chemko also significantly higher frequency of thy (incomplete abstract) (Langer et al, 1996)

Study #14

- no relation between PCB and thyroid hormone or creatine kinase and thyroid hormone was observed

18.9% of the patients with Kanemi Yusho showed an elevation of serum creatine kinase, however, the cause is still unknown. The relation between exercise, dehydration, thyroid hormone and concentration of PCB was studied. Dehydration, hyperexercise and PCB affected the elevation of creatine kinase. No relation between PCB and thyroid hormone or creatine kinase and thyroid hormone was observed. PCB may change the permeability of muscle plasma membrane. (Yoshimura et al, 1997)

Study #15

- significant differences in thyroxine (T4) and T4-RT3 index, correlated with PCB exposure
- studied 111 workers, half exposed to PCBs

Thirty-eight transformer repairmen currently exposed to polychlorinated biphenyls (PCBs), 17 former transformer repairmen, and 56 comparison workers not known to be exposed to PCBs were studied. Measurements were made of serum liver function tests, gamma-glutamyl transpeptidase (GGT), lipid profile, thyroid function tests, and other serum biochemistry; hemoglobin; white cell count; 24-hour excretion of delta-aminolevulinic acid, porphyrins, 17-hydroxycorticosteroids and 17-ketosteroids; sperm count; spirometry; and antipyrine half-life to evaluate microsomal mixed function oxidase induction. The total exposed group differed significantly from the comparison group in albumin, LDH, T4, T4-RT3 index, and actual/predicted FEV1. Significant differences among all three exposure groups were seen for albumin, T4, T4-RT3 index, and 17-hydroxycorticosteroid excretion. Differences in FEV1 were attributable to smoking. Significant correlations between serum PCBs and serum lipids were removed by adjustment for co (incomplete abstract) (Emmett et al, 1988)

Study #16

- thyroid function was normal.
- studied 182 newborns

To determine whether neonatal neurologic function is adversely affected by seafood contaminants from maternal diet during pregnancy. One hundred eighty-two singleton term births were evaluated in the Faeroe Islands, where marine food includes pilot whale. Maternal serum, hair, and milk and umbilical cord blood were analyzed for contaminants. Levels of essential fatty acids, selenium, and thyroid hormones were determined in cord blood. Each infant's neurologic optimality score was determined at 2 weeks of age adjusted for gestational age, and predictors were assessed by regression analysis. Exposures to methylmercury and polychlorinated biphenyls were increased in relation to maternal seafood intake, as were omega3 fatty acid concentrations in cord serum. Thyroid function was normal. After adjustment for confounders, a 10-fold increase of the cord-blood mercury concentration was associated with a decreased neurologic optimality score of 2.0 ($P = .03$). This effect corresponds to a decrease in gestational age of about 3 weeks. Other indicators of the seafood diet had no effect on this outcome. Prenatal exposure to methylmercury from contaminated seafood was associated with an increased risk of neurodevelopmental deficit. Thus in this North Atlantic population, methylmercury constituted an important neurologic risk factor, although effects of other seafood components were not detectable. (Steuerwald et al, 2000)

Study #17

- thyroid changes occurred, consistent with PCB exposure

- 2 of 6 workers exposed to PCBs were affected

A walk through survey and medical examinations were conducted to determine exposures to polychlorinated-biphenyls (PCBs) and asbestos at the Babcock Wilcox facility (SIC-3443), Brunswick, Georgia, on May 18, 1982. The evaluation was requested by Boilermakers Union Local 901 for 45 electricians and maintenance workers. Medical examinations were given to 12 employees, 6 of whom had a history of exposure to PCBs. A questionnaire was administered to determine asbestos exposure. Pulmonary function tests were given to eight workers with potential asbestos exposure. For workers with potential PCB exposure, none exhibited typical skin lesions. Blood concentrations of PCB were within normal ranges. In two subjects, thyroid and liver changes occurred that were consistent with PCB exposure. In subjects evaluated for asbestos exposure, four had decreased vital capacity and three of these had chronic bronchitis. Soil samples contained between 4.8 and 110 parts per million PCBs. The authors conclude that it is likely that workers are exposed to soils containing PCBs and there is potential exposure to asbestos at the facility. The authors recommend that transformers be labeled clearly warning about PCBs. Employees with long potential exposure times to PCBs and asbestos should be monitored to determine the cause of the symptoms. (Williams et al, 1983)

Study #18

- thyroid results not clear (incomplete abstract)
- studied 224 newborns

Preliminary findings of a cohort study designed to reveal the effect of the in-utero exposure to organochlorines on the health status of Inuit newborns in the Kativik region of Quebec, Canada were presented. Evaluations included birth weight, height, head circumference, and thyroid stimulating hormone blood levels. Breast milk levels were used as an indirect measure of fetal exposure. A total of 224 births occurred between July 1989 and July 1990. Milk analysis was performed for 109 of the mothers. Statistically significant negative associations were found between the height of male Inuit newborns and the concentrations of chlorinated pesticides, polychlorinated biphenyls (PCBs), polychlorinated dibenzo-p-dioxins (PCDDs), and polychlorinated dibenzofurans (PCDFs). In female newborns, positive associations were found between birth weight and PCBs/PCDFs. In male newborns, the associations remained significant even when controlling for maternal factors such as gestational age. The authors note that the indirect estimation of fetal exposure to contaminants using mother's milk levels is less precise than a direct cord blood measurement even though levels were adjusted on a lipid basis. The authors suggest that studies be made to determine whether these

compounds act differently on the intrauterine development of males and females. (Dewailly et al, 1993)

Study #19

- abstract incomplete

Objective: To evaluate whether long-term exposure to heavy environmental pollution with polychlorinated biphenyls (PCBs) could result in impairment of thyroid status as evaluated by an epidemiological field survey. **Methods:** Thyroid volume (ThV) was measured by ultrasound in 238 employees of a factory (EMP) which previously produced PCBs and 454 adolescents from the surrounding area polluted by PCBs. Controls (C) were 572 adults and 965 adolescents from much less polluted areas. In the 238 EMP and various numbers (shown in parentheses) of adult C the levels of thyroid-stimulating hormone (TSH) (n = 498), thyroxine (n = 498), thyroglobulin (n = 278) and thyroid antibodies (anti-peroxidase (TPO Ab), n = 517; anti-thyroglobulin (Tg Ab), n = 455; anti-TSH receptor (TSHR Ab), n = 238) were estimated in serum, while only TSH and TPO Ab were measured in 269 and 171 adolescents from polluted and control areas respectively. In several subjects in whom thyroid disease was suspected, total tri-iodothyronine or free t

(abstract incomplete) (Langer et al, 1998)

Study #20

- more research is needed, to include thyroid status

Half of a cohort of 3683 Michigan residents exposed to polybrominated biphenyls (PBBs) in 1973 and 1974 had 2 serum PBB determinations at a 1- or 2-yr interval. The median decrease in serum PBB levels during both 1- and 2-yr intervals was 1 microgram. The geometric mean serum polychlorinated biphenyl (PCB) level (6.3 microgram/L) exceeded that of PBB (4.1 micrograms/L), although the range of PCB levels (smaller than 1-57 microgram/L) was narrower than that of PBB levels (smaller than 1-3150 micrograms/L). Mean PCB and PBB levels were higher for males, and mean PCB levels increased with age. In a subgroup with higher-than-average PBB levels, serial clinical chemistry tests during 4 different years showed no consistent significant correlation with serum PBB levels. Tests with greater sensitivity and specificity for hepatic microsomal enzyme induction and thyroid status are needed in future evaluations of the most highly exposed subgroup of the cohort. (Kreiss et al, 1982)

February, 1999 -- The February 11, 1999 issue of the *New England Journal of Medicine* reports on the results of research that found that "treatment with thyroxine plus triiodothyronine improved the quality of life for most [hypothyroid] patients."

The article is titled:

"Effects of Thyroxine as Compared with Thyroxine plus Triiodothyronine in Patients with Hypothyroidism"

by Robertas Bunevicius, Gintautas Kazanavicius, Rimas Zalinkevicius, Arthur J. Prange, Jr.. Research was conducted by the Institute of Endocrinology, Kaunas Medical University, Kaunas, Lithuania along with the Department of Psychiatry, School of Medicine, University of North Carolina, Chapel Hill.

How the study was conducted

Essentially, they took a group of 33 people who were hypothyroid, either due to autoimmune thyroid disease, or removal of their thyroids due to thyroid cancer. All the patients were studied for two five-week periods. During one five-week period, the patient received his or her regular dose of levothyroxine alone. (Levothyroxine is the generic name for the brand names such as Euthyrox, Levoxyl, Levotheroid and Synthroid.) During the other five-week period, the patient received levothyroxine PLUS triiodothyronine (T3.) (Note: In the U.S., the brand name for T3 is "Cytomel.") In the T4 plus T3 phase, 50 µg of the patient's typical levothyroxine dose was replaced by 12.5 µg of triiodothyronine (T3). A variety of blood, cognitive, mood and physical tests were conducted at various stages of the testing.

Results

From the standpoint of physiological effects, the differences between pulse, blood pressure, reflexes and a variety of other functions for T4 alone, versus T4 plus T3, were very small. Blood pressure and cholesterol in fact dropped slightly on the T4 plus T3.

Where the results were dramatic were in mental functioning. Patients performed better on a variety of standard neuropsychological tasks on the T4 plus T3. Patients' psychological state also showed improvement on T4 plus T3.

At the end of the study, patients were asked whether they preferred the first or second treatments. 20 patients said they preferred the T4 plus T3 treatment, 11 had no preference either way, and only 2 preferred T4 only. The 20 patients who preferred T4 plus T3 reported that they had more energy, improved concentration, and just felt better overall.

The researchers determined that "treatment with thyroxine plus triiodothyronine improved the quality of life for most patients."

The researchers also recommended that the ideal thyroid hormone replacement program for someone without a thyroid gland, or whose thyroid gland is nearly non-functioning, would be "10 µg of triiodothyronine daily in sustained-release form. . . along with enough thyroxine to ensure euthyroidism."

Implications for Your Treatment

This study has major implications for people who don't feel well on their current thyroid hormone replacement.

If you are on standard levothyroxine only therapy, it's possible that, like the majority of study subjects, you too could feel better with the addition of a time-release T3 product in the recommended dosage ratio.

If you are on Armour Thyroid or Thyrolar, the current percentages of T3 in those drugs may be somewhat too high, compared to the recommended ratios described in this study. Optimal results may be obtained by modifying the treatment regimen to conform more specifically to the recommended ratio described in this article.

If you are on thyroid hormone replacement and don't feel well, I recommend that you notify your doctor right away about this research study, and get a copy of this article for yourself as well.

If you are going to share any information with your doctor, at the same time, you might also want to share a copy of a [British Medical Journal article](#) that suggests that values above TSH of 2 may not be "normal," but in fact represent abnormal levels indicative of a

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BMJ 1997;314:1175 (19 April)

Clinical review

Fortnightly review: Hypothyroidism: screening and subclinical disease

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At first sight there could hardly be a more simple disorder to diagnose and treat than hypothyroidism. Now that we have robust hormone assays and reliable preparations of thyroxine in tablet sizes sufficiently small to tailor doses to an individual's requirement, what issues remain? The purpose of this review is to flesh out some of the recently published consensus views on hypothyroidism,^{1 2} in particular regarding the role of screening for hypothyroidism and the need for treatment in subclinical hypothyroidism. Table [1](#)) gives the definitions of hypothyroidism.

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Table 1 **Definitions of hypothyroidism**

I have conducted a monthly Medline search for all articles on hypothyroidism for five years. For this review I scanned these papers and background papers for a recent consensus statement,² together with their references, for those focusing on screening and subclinical hypothyroidism. In addition, as part of my 15 years of thyroid related research I have continuously reviewed the literature.

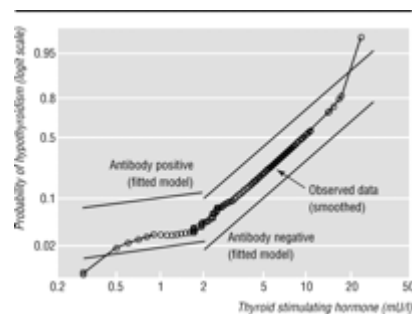
▶ **Frequency of hypothyroidism**

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New information on the frequency of hypothyroidism has been provided by a survey of a randomly selected population of 2779 adults living in Whickham, Tyne and Wear, who

had baseline thyroid function tests and were then reexamined after 20 years.³ Remarkably, 96% of the 1877 survivors participated in a follow up survey and 91% had further tests. The mean incidence of spontaneous overt hypothyroidism in women was 3.5 survivors/1000/year and in men 0.6/1000/year. There was no apparent excess of hypothyroidism in those who had died. The mean average at diagnosis was 58-59, but the probability of developing hypothyroidism increased steadily with age, reaching 14 cases/1000/year for women aged 75-80.

This survey also clarified the predictive value of detecting thyroid antibodies (against thyroid peroxidase/microsomal antigen) and measuring thyroid stimulating hormone concentrations. For women with subclinical hypothyroidism but without thyroid antibodies the relative risk of developing overt hypothyroidism over the follow up period was 8; the risk was the same for those with thyroid antibodies and normal thyroid stimulating hormone concentrations. Women with both increased thyroid stimulating hormone concentrations and thyroid antibodies had a relative risk of 38. Relative risks were even higher in men. Furthermore, even within the reference range of around 0.5-4.5 mU/l, a high thyroid stimulating hormone concentration (>2 mU/l) was associated with an increased risk of future hypothyroidism (fig 1). The simplest explanation is that thyroid disease is so common that many people predisposed to thyroid failure are included in a laboratory's reference population, which raises the question whether thyroxine replacement is adequate in patients with thyroid stimulating hormone levels above 2 mU/l. The high frequency of overt and subclinical hypothyroidism observed raises another contentious issue—namely, whether screening for hypothyroidism is worth while.



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Fig 1 Logit probability (log odds) for the development of hypothyroidism in women during a 20 year follow up of 912 women.³ Reproduced with permission

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General population screening

Screening for congenital hypothyroidism is definitely worth while as it is relatively common (1:4000 births), the test is sensitive and specific (thyroid stimulating hormone measurement in heel prick specimens), it has serious consequences if untreated (brain damage), and effective treatment is available (thyroxine). However, screening for hypothyroidism in hospital patients is not effective.^{4 5} Although undiagnosed hypothyroidism is more common in adults than neonates, the non-specific effects of acute illness on thyroid function tests often produce abnormal results which correct themselves after recovery. The best current recommendation is to maintain a low threshold for suspecting hypothyroidism, particularly in its more obscure presentations, and to reserve testing for these patients.⁵

In apparently healthy people routine screening is generally not recommended, even in those over 60 and with a family history of thyroid disease.^{2 4} Reasons for this include a relatively low point prevalence of overt disease and uncertainty over the benefits of detecting subclinical hypothyroidism (see below). However, a cost utility analysis using a computer decision model to assess the consequences and costs of thyroid stimulating hormone screening recently came to the conclusion that testing 35 year old men and women, with repeat estimates every five years for 50 years, would be beneficial.⁶

The cost of detecting subclinical hypothyroidism was \$9223 (£6148) for women and \$22 595 (£15 063) for men per quality adjusted life year.⁶ Most of the quality adjusted life years (52%) were accounted for by preventing progression to overt hypothyroidism and 30% by improving associated mild symptoms; 2% were estimated to be due to prevention of cardiovascular disease through the effect of hypothyroidism on cholesterol concentrations. This last estimate may be too high as the 20 year Wickham survey found no evidence of increased mortality or ischaemic heart disease in women with thyroid antibodies or raised thyroid stimulating hormone concentrations.⁷

Another assumption in the model was that only those patients with subclinical hypothyroidism plus thyroid antibodies are at risk of progression to overt hypothyroidism. Since raised thyroid stimulating hormone alone is a predictor of overt hypothyroidism, more cases at risk will be ascertained (which in turn will alter costs). Nevertheless, the final conclusion was that screening for hypothyroidism is as favourable as screening for hypertension in the same age group, providing a similar increase in quality adjusted days. It is also important to note that screening based on thyroid

stimulating hormone concentrations will of course also turn up subclinical and overt thyrotoxicosis,⁸ and arguably this is even more important to recognise and treat.

Further analyses based on existing local screening schemes are therefore needed to determine the true place of thyroid stimulating hormone testing for the general population. At present the benefits remain debatable. One reasonable alternative is the case finding approach, focusing testing on patients visiting their doctors for an unrelated reason; this is particularly effective in women over 40 with non-specific symptoms.⁴

Screening in special groups

Hypothyroidism occurs after all types of treatment for hyperthyroidism, and patients who are euthyroid should be offered annual screening by means of a computerised register (box).² Patients taking lithium or amiodarone are at risk of hypothyroidism and thyrotoxicosis and need regular monitoring of thyroid function.²

Summary points

Subclinical hypothyroidism is common, especially in elderly women

The presence of subclinical hypothyroidism or thyroid antibodies increases the risk of developing overt hypothyroidism and the risk is even greater (about 5% a year) if both are present together

Thyroid stimulating hormone concentrations above 2 mU/l are associated with an increased risk of hypothyroidism

Screening all acutely ill patients or the healthy general population for hypothyroidism is not recommended

Case finding, especially in women over 40 with non-specific symptoms, is currently the best approach to detect previously unsuspected hypothyroidism

Modest symptomatic benefits occur with thyroxine treatment in some patients with subclinical hypothyroidism, and lipid profiles may also improve

Monitored thyroxine treatment, maintaining normal thyroid stimulating hormone concentrations, has no adverse effects

There is no consensus on the place of screening for postpartum thyroiditis.⁹ However, women with insulin dependent diabetes mellitus are three times more likely to develop postpartum thyroid dysfunction than non-diabetic controls and may have unsuspected thyroid disease in pregnancy.¹⁰ Ideally, all diabetic women should have thyroid antibody measurements in the first trimester, with careful follow up of those with positive results. Also, any woman who develops postpartum thyroiditis should be offered annual follow up, as about a quarter of these women will develop overt hypothyroidism within the next five years.¹¹

Some psychiatric disorders may be exceptions to the rule that acutely ill patients should only be tested for hypothyroidism if there is clinical suspicion, in particular bipolar affective disorder with rapid cycling¹² and refractory depression.¹³ The effect of thyroid treatment in these conditions is still uncertain. Delaying testing until the third week after admission avoids the transient disturbances due to the effects of acute psychiatric illness.¹⁴ Although frequently sought in dementia, unsuspected hypothyroidism is rare.⁴ There is an unexplained association between breast cancer and autoimmune (Hashimoto's) thyroiditis, with a threefold increase in the prevalence of thyroid antibodies, and it may be worth screening such patients for thyroid dysfunction.¹⁵

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A big argument in favour of screening is that recognition and treatment of subclinical hypothyroidism is beneficial.⁶ At first sight this seems paradoxical because free thyroxine concentrations are normal and some regard the exclusion of symptoms as a criterion for diagnosis (table 1).²⁻⁸ However, many patients do have non-specific symptoms, such as tiredness and weight gain, which could be due to hypothyroidism. After all, the thyroid function tests needed to establish the biochemical diagnosis have usually been performed because of this suspicion. Also, after treatment with thyroxine the patient may notice an improvement in symptoms previously unrecognised because of the slow progression of thyroid failure and its variable manifestations. As thyroid stimulating hormone concentrations above 2 mU/l reflect a disturbance of the thyroid-pituitary axis (fig 1), values above the upper level of the typical reference range (4.5 mU/l) are highly significant departures from normal rather than one tail of the normal distribution. Is there any hard evidence that these patients benefit from early treatment?

Effect on neuropsychiatric and other symptoms

One small crossover trial has indicated that thyroxine improves symptom scores (including mental lethargy) and psychometric performance compared with a placebo.¹⁶ This trial is supported by a study which included patients previously treated for hyperthyroidism¹⁷ and by a prospective, unblinded trial of thyroxine in patients with subclinical hypo- thyroidism.¹⁸ More tenuous is the evidence that subclinical hypothyroidism is common in affective disorders, as such observations have been uncontrolled or the effects of thyroxine replacement have not been assessed.^{19 20 21}

Postpartum symptoms of depression are more common in women who have thyroid antibodies than in those without irrespective of biochemical thyroid dysfunction.²² Also,

in patients with rapid cycles of a bipolar affective disorder the most significantly associated thyroid disorder was thyroid antibody positivity and not raised thyroid stimulating hormone concentration.¹² Whatever the reason, the implication is that some mood disturbance in subclinical hypothyroidism has an immunological rather than an endocrinological basis, in which case thyroxine treatment would not help.

Effect on lipids

The adverse effects of subclinical hypothyroidism on cholesterol concentrations have been promoted as a reason for screening and treatment.^{6 23} A recent study found an association of subclinical hypothyroidism not only with raised low density lipoprotein cholesterol and low high density lipoprotein cholesterol concentrations but also with raised lipoprotein(a).²⁴ Although hypothyroidism theoretically increases the risk of cardiovascular disease, there is no evidence that thyroxine will reverse this potential and, indeed, any such risk must be small, given the results from the Whickham survey.⁷ The effects of thyroxine replacement on cholesterol lowering alone are modest. A re-analysis of intervention studies between 1976 and 1995 led to the following conclusions²⁵:

- **Subclinical hypothyroidism is two to three times more common than expected in people with increased total plasma cholesterol concentrations**
- **Total cholesterol is only slightly raised (0-30% above normal) in subclinical hypothyroidism.**

Indications for screening for hypothyroidism

Established

Congenital hypothyroidism

Treatment of hyperthyroidism

Neck irradiation

Pituitary surgery or irradiation

Patients taking amiodarone or lithium

Probably worth while

Type 1 diabetes antepartum *

Previous episode of postpartum thyroiditis

Unexplained infertility

Women over 40 with non-specific complaints

Refractory depression; bipolar affective disorder with rapid cycling

Turner's syndrome; Down's syndrome

Autoimmune Addison's disease

Uncertain

Breast cancer

Dementia

Patients with a family history of autoimmune thyroid disease

Pregnancy, looking for postpartum thyroiditis *

Obesity

Idiopathic oedema

Not indicated

Acutely ill patients with no clinical reason to suspect thyroid disease

*** Check thyroid antibodies; screen positive patients post partum using thyroid stimulating hormone.**

Other effects

Minor alterations in heart muscle contractility, determined by systolic time intervals, occur in around half of patients, although not all studies agree.⁸ Only a subgroup with the most serious abnormalities improves with thyroxine replacement.¹⁷ An asymptomatic polyneuropathy can be identified in subclinical hypo- thyroidism,²⁶ but the response to treatment has not been analysed and the clinical impact of this is even less clear than for alterations in myocardial function. One potentially important adverse effect of subclinical hypothyroidism is to alter the dynamics of prolactin release, with unknown consequences for gonadal function and fertility.²⁷ Testing for thyroid disease seems warranted in all women and men with unexplained infertility.

Another argument in favour of instituting thyroxine replacement is that it prevents the onset of overt hypothyroidism. This is particularly persuasive for people with raised thyroid stimulating hormone concentrations plus thyroid antibodies, who have an annual risk of developing overt hypothyroidism of around 5%.³ Practically, however, the patient is probably not spared many follow up visits in return for starting thyroxine early. This is because thyroxine dose requirements are less in subclinical hypothyroidism than in overt disease, and so careful monitoring is needed until the normal replacement dose is reached (100-150 µg daily). At this time checks every one to three years can be instituted, provided that thyroid stimulating hormone concentrations are normal and stable.

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Are there risks from taking thyroxine which argue against treating subclinical hypothyroidism? Providing thyroid stimulating hormone concentrations are restored to the reference range, the answer is no, and even if too much is given, the risks of osteoporosis are more theoretical than real. A meta-analysis of studies of excessive thyroxine treatment found no reduction in bone mass in premenopausal women, although postmenopausal women had a significant excess annual bone loss of 0.9%/year after 10 years.²⁸ However, no increased rate of fractures occurs, despite this loss, and it is also important to distinguish those who are taking thyroxine for iatrogenic hypothyroidism from those with spontaneous hypothyroidism: in the first group there has usually been a period of hyperthyroidism which contributes to the bone loss.²⁹

The other main concern is the action of excessive thyroxine on the heart. Subclinical hyperthyroidism in people aged 60 or older is associated with a trebling of the risk of atrial fibrillation over 10 years.³⁰ It is not clear whether the risk applies equally to patients

taking thyroxine for iatrogenic hypothyroidism and those with spontaneous hypothyroidism. This study is the most persuasive reason to maintain normal thyroid stimulating hormone concentrations in all patients receiving thyroxine, whether for subclinical or overt hypothyroidism. On balance, the risks of properly monitored thyroxine treatment are almost non-existent.

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Clinical and subclinical hypothyroidism are common. The presence of either a raised thyroid stimulating hormone concentration or thyroid antibodies indicates an increased risk of future hypothyroidism and this is greater when both occur together. Screening for hypothyroidism may be more cost effective than usually presumed and certain subgroups at risk can be identified, but further work is needed to establish the optimum strategy. On the other hand, the high frequency of abnormal thyroid function test results in acutely ill patients means that any testing should be reserved for those in whom there is clinical suspicion of thyroid dysfunction. There are modest benefits from treating subclinical hypothyroidism, and figure 2) suggests a management strategy.



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Fig 2 Algorithm for managing non-iatrogenic subclinical hypothyroidism. Thyroid peroxidase antibodies alone are

recommended for screening as thyroglobulin antibodies rarely occur in the absence of these antibodies²

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Are there any particular supplements you think most people with hypothyroidism should probably be taking?

A. I am not a huge fan of supplements and encourage most people to optimize their diet. I have an [outline](#) that I have all my patients follow and it is a good starting point. The nutritional changes help to optimize their insulin levels, which have an important element to normalizing the biochemistry that generally goes along with chronic illness.

But for specific recommendations for hypothyroidism, I feel the best supplement that one

could possibly take for proactive thyroid health on a regular basis would be some form of organic iodine. A simple way to determine if one requires this is to paint a patch of tincture of iodine on your skin the size of a half dollar. The iodine brown coloration should last at least 24 hours. The faster it is absorbed the greater the body's iodine deficiency.

The best source of organically bound iodine that I know of is non-commercially harvested seaweeds. The dose is about 5 grams a day or about one ounce per week. So a pound would last about two months. Radioactive iodine is another factor that can damage the thyroid so one needs to flood the gland with healthy iodine from organic sources like seaweed. As you know this is particularly important for pregnant women as if they have untreated hypothyroidism their, a New England Journal of Medicine study showed that their children may have lower IQ scores.

The better seaweeds are hand picked and dried and not typically available in health food stores. They are the absolute best forms of minerals that I am aware of. Unfortunately the people who produce this usually run small operations, and do not make their products widely known. Kelp from the health food store may work, but it really depends on how it was harvested and there is no way to know that reliably, so I rely on seaweed harvesters who hand pick the seaweed and reliably dry them free from contaminants.

If one already has a thyroid problem the issue is far more complicated. It is difficult to make general recommendations without identifying the underlying cause of the individual's hypothyroidism. One of the most common is psycho-emotional stress that impairs the adrenal glands from working properly. Once the adrenals are compromised the thyroid gland attempts to compensate for the exhausted adrenals and the thyroid frequently loses its ability to function normally. I have four psychotherapists in my center who work on this issue using very sophisticated autonomic nervous system rebalancing that incorporates multiple forms of [muscle testing](#).

Mercury is another common cause of hypothyroidism. Amalgams are 50% mercury and they are only inches away from the thyroid gland. If diagnostic testing determines mercury to be a problem then the amalgam fillings need to be removed by a biologically trained dentist and replaced with a non-metal (composite) filling. The mercury needs to be eliminated. I have written with Dr. Dietrich Klinghardt a comprehensive protocol for this that will be published shortly. A [short summary](#) of the protocol is on my web site.

Q. What are your thoughts about "Wilson's Syndrome," which uses body temperature as the sole means of diagnosis, and uses primarily T3 only as a treatment?

A. First of all traditional medicine already has established Wilson Disease (hepatolenticular degeneration). It was first described in 1912 as a problem resulting in copper accumulation in the liver and brain. Wilson Disease has to do with a reduction in the incorporation of copper into its transport protein, ceruloplasmin. This results in copper deposition in the cornea, brain and basal ganglia. Clearly this disease predates the Wilson syndrome, and although Wilson Syndrome and Wilson Disease are different names, I believe they are too similar and am surprised that someone would be so audacious to name a disease syndrome after himself that is so easily confused with a well defined existing medical entity.

Some have commented that his book for the public is of the worst of vanity-press publishing, although his doctor's manual is surprisingly well written and espouses some clever arguments, albeit based on some false premises. A previously interviewed clinician on your site, [Dr. John Lowe](#), does a great job pointing this out in his book.

The Wilson protocol is so complicated and time-consuming to follow that it requires a truly unusual patient and more time than a physician can usually afford to have any

chance of being executed properly. Unfortunately, until patients encounter something better, legions of desperate patients, incorrectly treated by the "endocrinologist-thyroidologist technocracy" have clung onto the hopes provided by Dr. Wilson's book. That is what you offer on your wonderful site, the chance to learn superior alternatives to the Wilson Syndrome complicated and generally non-effective approach.

However, giving credit where credit is due, Dr. Wilson's thoughts about "compensation" effects (and the differences therein among different patients) are useful and based on good logic and probably some quite astute clinical observations. Indeed, these dynamics are pertinent to what happens before a patient taking T3 stabilizes, and an awareness of this process may be a useful nugget to salvage from the considerable time many of us have invested into studying Wilson's approach. Of course, that does not suggest in any way that Wilson's cycling protocol with enormous doses of T3 has any merit or should be used.

Q. A major complaint many people with hypothyroidism have is difficulty losing weight, even after they've been diagnosed, and are on optimum amounts of thyroid hormone, including T3. Do you have any suggestions for those people who are finding it particularly difficult?

A. Absolutely. This typically is easily resolved if the patient is compliant, as I have guided hundreds of patients through this process successfully. The central issue is compliance as my observation is that most people have an emotional issue that complicates optimal resolution of this problem. The first issue would be to abandon the traditional viewpoint that [grains are healthy for most of us](#).

Grains convert to sugar and [cause profound disturbances in insulin balance](#) that lead to weight gain. I have a [diet plan](#) that I have put together over the years that seems to help most people in this area.

The second essential issue is that cardiovascular exercise is vital. Typically [one hour per day](#), each and every day is required, until ideal weight is achieved. The one-hour can be split into two or three sessions and the exercise needs to be relatively intense. I explain to patients it should be just below the threshold where they lose the ability to talk comfortably to someone standing next to them. If they can talk easily they are not working out hard enough. Of course one needs to gradually build up to this level and have clearance from their physician if they have heart disease.

Q. In researching my book, I talked to a number of scientists who felt that overconsumption of [soy isoflavones can create some health problems, including an increased risk of hypothyroidism](#). Do you have any thoughts about the current soy craze, and the pros and cons of soy consumption, including soy foods, and soy protein powders, and isoflavone supplements?

A. Once again Mary, you are right on target. There are very few professionals or media who understand this issue, and you are one of them. Dr. Enig is professor of biochemistry at the University of Maryland and is the researcher who brought trans fatty acid to the public's attention a few decades ago. I have a [15-page review](#) by Dr. Enig, which is the best summary I have seen on the subject. I believe the soy issue is one of the biggest health misconceptions in the natural food movement today and I plan on doing some national TV interviews on this subject soon. 20/20 is the first media to begin to expose the problem and had a [story with the soy infant formula](#) on June 9 of this year. I believe soy formula is one of the worst foods on the planet for an infant and should be banned. It provided the hormone equivalent of five birth control pills a day and may be one of the reasons infertility and other female endocrine problems are so common today.

Q. Some experts are concerned that the [fluoridation of water may be contributing to an increase in thyroid problems](#), among other health concerns. What are your thoughts about this? A. This is

a very controversial area. One of my friends, Dr. Ted Spence, did an [excellent review on this fluoride controversy](#) and I also have [many links](#) where one can explore this area in great detail. I believe fluoride, like mercury, is a chemical toxin and poison and should be avoided. There is likely to be a direct antagonism with iodine that is [well documented](#). I suspect most other logical and open individuals would reach the same conclusion if they critically analyzed the evidence.

Q. Do have any thoughts for patients who are having difficulties getting properly diagnosed or treated? People who cannot necessarily travel to see you, or who do not have access to doctors who are particularly savvy about thyroid treatment, and who are stuck with HMOs or who are limited to particular doctors with particular insurance plans?

A. Another excellent question. Like you, I receive 1,000 emails a week and I have long ago passed my ability to personally respond to all of them. The simple solution would be to ask every employee of a health food store for a medical doctor that practices natural medicine. Nearly every community has one, although you might have to travel somewhat. I would ask the storeowner and all the employees, don't just ask one part-time employee, be persistent and contact all the health food stores in your area. They are tremendous local resources.

If that option fails I would call the American College for the Advancement of Medicine (ACAM 714-583-7666). I am a member of this group and most of these physicians are open to using natural hormones. I would just give them a copy of the information on my web site regarding thyroid hormone diagnosis and management. If the ACAM physician had any questions I would be glad to answer them and help guide them through the process. But most of them are already using Armour thyroid, they just may not be familiar with the revised use of the Free T3 and Free T4 levels.

Q. Is there anything else you'd like to share about your thoughts on hypothyroidism?

A. I would encourage readers to be persistent. It has been my experience that the vast majority of "thyroid experts" including some of the ones listed on your site, are not in agreement with the material I have reviewed here. Readers need to be convinced that there is a solution that addresses the cause for many of their chronic health care complaints, despite the traditional medical paradigm insistence that there is not.

If one already has thyroid failure, then it is not possible to return the gland to normal and readers should seek a form of therapy that optimizes T3 levels. For the vast majority of patients levothyroxine (Synthroid) does not achieve this. I see many patients who have searched long and hard to find a physician who was willing to give them a thyroid replacement like Armour thyroid. It is my experience that once these individuals change their thyroid replacement to a natural thyroid product their quality of life soars.

For the past 25 years, tens of millions of Americans in hundreds of cities and towns have been drinking tap water that is contaminated with low levels of insecticides, weed killers, and artificial fertilizer. They not only drink it, they also bathe and shower in it, thus inhaling small quantities of farm chemicals and absorbing them through the skin and through breathing in the vapors. Naturally, the problem is at its worst in agricultural areas of the country. [Pesticides have been shown](#) to interfere with thyroid function and [cancer risk](#), so it is imperative to drink clean water.

Biochem Pharmacol. 1997 Nov 15;54(10):1087-96. [Related Articles](#), [Links](#)

[ELSEVIER SCIENCE
FULL-TEXT ARTICLE](#)

Anti-thyroid isoflavones from soybean: isolation, characterization, and mechanisms of action.

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The soybean has been implicated in diet-induced goiter by many studies. The extensive consumption of soy products in infant formulas and in vegetarian diets makes it essential to define the goitrogenic potential. In this report, it was observed that an acidic methanolic extract of soybeans contains compounds that inhibit thyroid peroxidase- (TPO) catalyzed reactions essential to thyroid hormone synthesis. Analysis of the soybean extract using HPLC, UV-VIS spectrophotometry, and LC-MS led to identification of the isoflavones genistein and daidzein as major components by direct comparison with authentic standard reference isoflavones. HPLC fractionation and enzymatic assay of the soybean extract showed that the components responsible for inhibition of TPO-catalyzed reactions coeluted with daidzein and genistein. In the presence of iodide ion, genistein and daidzein blocked TPO-catalyzed tyrosine iodination by acting as alternate substrates, yielding mono-, di-, and triiodoisoflavones. Genistein also inhibited thyroxine synthesis using iodinated casein or human goiter thyroglobulin as substrates for the coupling reaction. Incubation of either isoflavone with TPO in the presence of H₂O₂ caused irreversible inactivation of the enzyme; however, the presence of iodide ion in the incubations completely abolished the inactivation. The IC₅₀ values for inhibition of TPO-catalyzed reactions by genistein and daidzein were ca. 1-10 µM, concentrations that approach the total isoflavone levels (ca. 1 µM) previously measured in plasma from humans consuming soy products. Because inhibition of thyroid hormone synthesis can induce goiter and thyroid neoplasia in rodents, delineation of anti-thyroid mechanisms for soy isoflavones may be important for extrapolating goitrogenic hazards identified in chronic rodent bioassays to humans consuming soy products.



Thyroid History

Salem 1945

Klein

Flashbacks

Toothpaste

Thyroid History

History of the Fluoride/Iodine Antagonism

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see also: [Antagonism](#)

1854 - Maumene feeds sodium fluoride to a dog and causes a goitre to appear [*a goiter*]. He is the first to consider fluorides as a cause of goiter.

1869 - First experiments with sodium fluoride, showing inhibitory effects on [glycogen](#) *thyroid hormone - regulated event*] in isolated muscle tissue, are published by Na *also: 1937 Litzka*)

1918 - [McKay](#), the dentist who discovered that fluoride causes mottled teeth, writes "Dental Cosmos" that enamel conditions in children with 'mottled teeth' - later to be renamed 'dental fluorosis' - are identical to those reported by Prof. Greves in Holland, being due to thyroid dysfunction (goiter).

1923 - Pighini causes goiters with fluoride in rats, dogs and chicken.

1926 - Goldemberg (Argentina) is the first to take medical advantage of the mucous iodine-fluoride [antagonism](#). He investigates the areas then commonly referred to as "goiterous waters" ('Kropfwaesser'), and reviews the work by others (*Repin, Gau, Clausmann, McCarrison, Parhou and Goldstein, Pighini, Christiani, Cahages, Hous, Tappeiner, Schulz, Brandt and Pisotti*). His findings convince him that the world-wide occurrence of goiter and cretinism is NOT due to iodine deficiency as commonly believed but to excessive fluoride intake from air, food and water. He reasons that fluorides therefore also reduce the high iodine levels in Basedow patients and begins to use them to effectively cure Basedow's disease (Graves' Disease), a disease thought to be caused by excessive iodine consumption.

Based in Buenos Aires, Goldemberg publishes extensively between 1921 and 1930 his findings of applying fluorides as anti-thyroid medication.

1927 - Gorlitzer von Mundy (Austria) reports that daily intake of 3 mgs of fluoride in mice and rats leads to goiter and cretinism-like conditions.

1930 - Christiani publishes on the changes in thyroid function from fluoride injection [*Earlier, in 1925, Christiani and Gautier became the first to use the term 'fluorosis' and called it "La Fluorose" and "Cachexie fluorique", using these terms to describe "fluorine intoxication" (not yet described as "dental fluorosis"...), as induced by fluoride emanating from a Swiss aluminum smelter. [LINK](#)*]

1932 - Gorlitzer von Mundy (Austria) publishes findings on 1500 experiments using fluoride to inhibit thyroid function in mice and metamorphosis in tadpoles.

- **NOTE: As it had been shown that metamorphosis in tadpoles was regulated by thyroid hormones, one had to show inhibition of metamorphosis to satisfy claims that a medication was an "anti-thyroid". This test was known as the "Gudernatsche [Tadpole Test](#)".**

1932 - Machoro (Italy) uses sodium fluoride in the successful treatment of hyperthyroidism.

1932 - Wilhelm May (Germany) also starts fluoride therapy in the treatment of hyperthyroidism, using calcium fluoride tablets, topical ointments, etc.

1933 - Gorlitzer von Mundy (Austria) reports more on fluoride's effect on the thyroid.

1934 - Purjesz and colleagues (Poland) give chicken eggs high in fluoride to hyperthyroid patients and achieve lowering of body temperature, of pulse and BMR, as well as weight gain; report that most of the fluoride is found in liver; **no** fluoride is found in the thyroid of healthy people.

1935 - Phillips et al. (USA) report that fluoride and thyroid have synergistic effects on the development of fluorosis in chicken.

1935 - Phillips et al. conduct studies in rats and find the same results: fluoride and thyroid have synergistic toxic effects.

1936 - Phillips conducts further animal experiments and verifies the 1935 findings.

1937 - Litzka (Germany) discusses the mode of action of fluorides in treating patients with hyperthyroidism: fluoride antagonizes thyroid hormone effects/glycolysis in liver and also influences glycolysis in skeletal muscle.

1937 - Wilhelm May reports further on his fluoride therapy, including the use of sodium fluoride ointments (up to one year-therapy), and Fluorotyrosin (6 to 8 - week therapy). He reports on findings that two other common medications given in the treatment of hyperthyroidism - *Solvitren* and *Tyronormin* - had been found to contain fluoride in amounts double the amount used in *Fluorotyrosin*. Further May reports that the traditional "Kur" where people had been sent for "natural therapy" ('Kur') were found to contain high amounts of fluoride in the water.

1937 - [Kraft](#) (Knoll AG, Germany) investigates inorganic *sodium fluoride* and organic fluoride compounds *fluorobenzoic acid* and *fluorotyrosine* and reports that all fluoride compounds inhibit thyroid hormones. It is a matter of amplification - the fluoride effect is essential.

1939 - Steyn (South Africa) first reports on his findings of fluoride-induced goiter.

1940 - Wilson and DeEds (USA) report dental fluorosis in rats as a result of the synergistic action of fluoride and thyroid hormones. Results are described as "strikingly clear".

1941 - Wilson (UK) reports in the *Lancet* on his findings that mottling of teeth is seen in the same areas in the UK which had previously been prevalent with goitre.

1941 - Schwarz (Germany) prepares fluoride/iodide anti-thyroid medications and combines them with sedatives.

1942 - Euler & Eichler (Germany) report that the chronic administration of organic fluoride compounds (*fluorotyrosine*) cause the same defects in bone as inorganic fluorides. No dissociation takes place, ascribing effects to the whole molecule.

1942 - Euler & Eichler further report that the chronic administration of organic fluoride compounds cause the same defects in teeth as inorganic fluorides. *Identical crystal formation is seen, although no soluble (free) fluoride is observed, leading to the automatic conclusion that such crystals declared by others to contain "calcium fluoride" [see [fluoroapatite](#)] could not be such. The organic compounds did not dissolve.*

1944 - The editorial in the *Journal of the American Dental Association (JADA)* acknowledges that "...drinking water containing as little as 1.2 to 3ppm of fluorine will cause such

developmental disturbances...as goitre".

1946 - The [Atomic Energy Commission](#) (*Department of Pharmacology & Toxicology*) headed by Harold Carpenter Hodge, incomprehensibly at the same time also head of the *International Association for Dental Research (IADR)* - acknowledges the German findings that all fluoride compounds - organic or inorganic - inhibit thyroid hormone activity and declares this issue a research priority. No further research into this issue is conducted, however.

1947 - Castera uses Knoll's "K17", later to be renamed "Capacin", in the successful treatment of 500 hyperthyroid patients.

1948 - Steyn (Africa) finds that fluoride has definite anti-thyroid effects. He investigates the incidence of endemic goiter in the North Western Cape Province in South Africa and reports that his findings "closely agree with the ... 1944 JADA editorial", and that goiters are actually 'fluoride-induced'.

1949 - Richard May reports on the highly successful use of the organic fluoride compound **Pardinon** (*IG Farben*) and **Capacin** (*Knoll AG*) in the treatment of hyperthyroidism. By 1943, 10,000 patients had been cured.

1949 - Euler et al. test various organic fluoride compounds and find again that all organic fluoride compounds inhibit thyroid hormone activity.

1950 - Wilhelm May publishes monograph on the fluoride-iodine antagonism, including 300 references, detailing the known [biochemical findings](#). [*Originally slated for publication in 1944, the lack of paper in Germany prohibits publication until 6 years later.*]

1950 - Richard May reports that between 1935 and 1947 over 5000 hyperthyroid patients had been treated successfully with *Pardinon* and *Capacin* in the May clinic alone.

1952 - Kraft and Dengel (Germany) investigate yet more *fluorophenyl*-derived fluoride compounds, all of which lower BMR.

1952 - In the court case Reynolds Metals Corp vs Paul Martin hypothyroidism caused by fluoride is documented.

1953 - Wadwhani (India) reports that fluoride concentrated in thyroid gland of rats after consuming 0.9mg F- per day.

1954 - Wespi (Italy) reports mottled teeth ('dental fluorosis') **together with goiter** in Italy.

1954 - Jentzer (Switzerland) reports that less than normal amounts of thyroid hormone are deposited in the pituitary gland when rabbits are given fluoride in water - at levels corresponding to that of artificially fluoridated water.

1955 - [Benagiano & Fiorentini](#) (Italy) describe the effects of fluoride on thyroid function. They find that the farther away from the toxic dose, the longer it takes for fluoride-induced thyroid changes. (*This in accord with May (1950), who found that although it might take months - "sometimes even a year" - even low fluoride amounts would always be effective in lowering iodine levels...May urged the practitioner to be patient...*)

1955 - Korrodi, Wegmann, Galetti and Held also verify a fluoride - iodine antagonism, presuming that the fluoride ion pushes out the iodine in the thyroid gland.

1957 - Galetti et al. treat hyperthyroid patients with fluoride at daily doses lower estimated being the current average intake in the US, and document a significant in protein-bound iodine, as well as an overall reduction of iodine and a reduction of uptake by the thyroid gland.

1959 - Jentzer again shows reduced iodine levels in the pituitary gland under the of fluorides.

1960 - Gordinoff and Minder describe the results of experiments with radioactive (I131) which show that fluorides remove an iodine atom during the conversion process to T3). Effects are dose-responsive, meaning the higher the fluoride intake the lower iodine measurements.

1959/1960 - Anbar et al (Israel) report in *Nature* and other journals that [fluoride](#) and other fluoride compounds inhibit thyroid hormone transport and concentrate in the thyroid gland. [BTW: *The first fluoroborate safety document appeared in 1932!*]

1962 - Steyn (Africa) reports that drinking water containing "as little as 1 to 2 ppm of fluorine can cause serious disturbances of general health and especially in normal thyroid gland function and in the normal processes of calcium-phosphate metabolism ([parathyroid function](#))."

1962 - Spira reports on the fluorine-induced endocrine disturbances in mental illness.

1963 - Gorlitzer von Mundy reports on the [then] current knowledge gained from experiments with I131 as to how the effects of the enzyme responsible for the T4 to T3 conversion were inhibited if a fluorine ion was absorbed before the conversion from T4 to T3 occurs.

1964 - Ritzel reports on disturbances in T4 metabolism in areas with fluoridated drinking water.

1964 - Steyn (Africa) - again - reviews the "overwhelming evidence" on the fluoride-iodine antagonism.

(Steyn, Maumene, Euler et al., Wadwhani, Wadwhani and Ramaswamy, Chang et al., Littich, Benagiano and Fiorentini, Fiorentini, Feltman, De Eds, Baume and Becks, Orban, Spira, Galetti et al., Gordonoff and Minder, Wilson, Wespi, Goldemberg, Todd, Coton, Gorlitzer, May, Hodenberg, Korrodi et al., Christiani, Jentzer, Grab and Overdisse)

1964 - Steyn reports on his detailed 1949-1950 experiments on young rats, conducted to determine if there was in fact a fluoride-iodine antagonism. The experiment, which lasted 12 months, showed that **the more severe the teeth were mottled, the more severe the thyroid dysfunction**. It further showed that iodine supplementation was not sufficient to prevent the endemic goitre caused by excessive fluoride in drinking water, and that the fluoride intake needed to be reduced.

1969 - Rodesch et al. and Zor et al. independently report that fluoride mimicks TSH.

1969 - Siddiqui show small visible goiters in persons 14 to 17 years of age in India, which are connected directly to high fluoride concentrations in drinking water.

1970 - Ahn and Rosenberg confirm that fluoride mimicks TSH.

1970 - Burke documents that TSH and fluoride have additive effects.

1971 - Narbutt et al. show that in rats fed sodium fluoride at 0.1 and 1 mg/day there is an increase in the thyroid weights after 4 weeks, irrespective of dosage. Narbutt recorded

iodine administration during fluoride prophylaxis.

1972 - Willems et al. document that sodium fluoride blocks thyroid hormone secretion.

1972 - Day and Powell-Jackson study 648 people in 13 mountainous regions in India where the iodine content in the water is low and find a close relationship between fluoride intake and the incidence of goiter.

1976 - Polish researchers [Bobek and Kahl](#) document that rats consuming fluoride at 0.1 to 1 mg/day have significantly lowered T4, T3, and free thyroxine index in blood. They ascribe this to an inhibition of thyroid hormone transport by fluoride.

1976 - Aliev finds that goiter, caries and fluorosis are correlated in Azerbaijan.

1976 - [Orgiazzi et al.](#) use fluoride as TSH analogue in assessing "cold nodules".

1978 - In German thyroid medications like "Druesensalbe Fides", "Strumadragee" and "Strumetten", calcium fluoride and hydrogen fluoride are still used as ingredients. Listed in the 1978 index of the German Federal Association of the Pharmaceutical Industry ("Schilddruesentherapie" in "Rote Liste", Bundesverband der Pharmazeutischen Industrie, e.V., Frankfurt, Germany)

1978 - [Maccia et al.](#) use fluoride as TSH analogue (*hyperplastic thyroid, hyperfunctional follicular carcinoma, "cold" nodules*).

1978 - [Kalderon & Sheth](#) use fluoride as TSH analogue (*"cold" nodules*).

1978 - George Waldbott writes that in most cases of poisoning from fluoridated water, which he had occasion to study the action of the thyroid gland, its function was low. He cites a case of a 33-year-old male who exhibited typical manifestations of pre-skeletal fluorosis and a basal metabolism rate of -22, indicative of hypothyroidism. Within 6 months after the man ceased consuming fluoridated water, the thyroid function had returned to normal (BMR=0). In addition, Waldbott writes that "simultaneously, all the symptoms associated with low grade fluoride poisoning - including excessive thirst, headaches, blurred vision, arthritis in shoulders, elbows, knees, and gastrointestinal disturbances - also disappeared." [*He did not know that the symptoms he ascribed to low grade fluoride poisoning" would likewise be considered symptoms of hypothyroidism 20 years later.*]

See: [COMPARISON OF SYMPTOMS: FLUORIDE POISONING/HYPOTHYROIDISM](#)

1979 - [Toccafondi et al.](#) use fluoride as TSH analogue in assessing hyperfunctioning thyroid (*thyroid toxic adenoma*).

1979 - [Walinder et al.](#) use fluoride as TSH analogue to activate human thyroid tumor (*nodules*).

1979 - [Hillman et al.](#) find that cattle afflicted with fluorosis develop hypothyroidism. (*Fluorosis here caused by mineral supplements.*)

1982 - [Mizukami et al.](#) use fluoride as TSH analogue (*adenomatous goiter*).

1983 - [Sidora et al.](#) find iodine deficiency and "adaptive amplification of the hypothyroid system, not ensuring an absolute compensation in the citizens using drinking water with an 'enhanced' fluorine content as compared to a 'decreased' one, accompanied by a 'decreased' iodine content."

augmented incidence of functional disturbance".

1983 - Desai et al.(India) report increased incidence of goiter in endemic fluorosis

1985 - [Bachinskii et al.](#) document how fluorides at 2.3 ppm in water cause tensic function of the pituitary-thyroid system that is expressed in TSH-elevated production and decrease in the T3 concentration [*both sure-tell diagnostic signs of hypothyroidism*]. The more intense absorption of radioactive iodine by the thyroid [*as in iodine deficiency*] results lead to a conclusion that excess of fluorine in drinking water was a risk factor for more rapid development of thyroid pathology.

1985 - [Clark and Gerend](#) use fluoride as TSH analogue in human thyroid cancers

1988 - Zhao publishes first results of investigations into mutual interactive effect of fluoride and iodine in goitre and dental fluorosis.

1988 - Guan et al. report on synergistic effects of iodine deficiency and fluoride exposure on rat thyroid.

1989 - [Tokar' and others](#) in a study on workers exposed to fluorides write that "changes in the pituitary-thyroid axis are caused by disorders of the regulatory chain and fluoride interference with thyroid hormones' metabolism at the level of target cells". (-> *G-proteins*)

1989 - Ren et al. report more findings on the devastating effects on IQ of fluoridated water in iodine areas.

1991 - [Lin Fa-Fu et al.](#) report that a low iodine intake coupled with "high" (0.88ppm) fluoride intake exacerbates the central nervous lesions and the somatic development disturbance of iodine deficiency. The authors considered the possibility that "excess fluoride ion affected normal de-iodination. Fluorides caused increase of reverse T3 (rT3) and elevated TSH levels, as well as increased I131 uptake (see: *Bachinskii et al, 1983*)

1991 - Delemer et al. show that fluoroaluminate (AlF₄⁻) and TSH have additive effects

1993 - Brtko et al. find that fluoride inhibits binding of 125I-T3 to its receptor in thyroid nuclei.

1993 - Desai et al. investigate 22,276 people in India and find dental fluorosis and iodine deficiency significantly and positively correlated.

1994 - [Tezelmann et al.](#) report that fluoride, by increasing the intracellular cAMP concentration, causes desensitization of the thyroid stimulating hormone receptor. No specific thyroid factor(s) other than increased levels of cAMP are required for TSH desensitization.

1994 - [Yang et al.](#) investigate intelligence in children and report that high iodine and fluoride exert "severe damage to the human body".

1995 - [Balabolkin et al.](#) study the thyroid and immune statuses in workers continuously exposed to fluorine. "...T3 is seen reduced in 51% of the workers. The examinees with 'euthyroid condition' had immune disorders with an allergic tendency (increased number of B-lymphocytes, immunoglobulins A). In workers with subclinical hypothyroidism, immune alterations were more evident, T-lymphocytes count rose, but their functional activity declined, indicating impaired cooperation of immunocytes as a result of imperfect control under low

concentrations of T3." (*aberrant G protein activation*).

1996 - Mikhailets et al. also report low T3 levels in workers exposed to fluorides.

1998 - [Zhao et al.](#) conduct an extensive study on mice receiving several fluoride-combinations in addition to basal diet. He finds that iodine and fluorine have "mutually interacting" effects on both goiter and fluorosis in the experimental mice.

1998 - [Swarup et al.](#), investigating fluoride-intoxicated cattle near an aluminum smelter in India, find decreased levels of triiodothyronine (T3) in the affected animals when compared to normal animals.

1999 - Data by [Jooste et al](#) shows that goitre occurrence in **iodine-sufficient** areas in Africa is due to fluoride. In 5 out of 6 villages goiter prevalence directly corresponds to fluoride in water, observable at concentrations even lower than deemed "optimal for caries prevention".

2001 - [Negoita et al.](#) report the increase of acquired hypothyroidism in the St. Regis Akwesasne Mohawks, a population long known to be poisoned by fluoride emissions from the Reynolds aluminum smelter.

2001 - 2002 - [Gupta et al.](#) (India) and [Suketa](#) (Japan) show that in cases of fluoride-induced hyperparathyroidism, as seen in elevated parathyroid hormone (PTH) levels.

It is now known that elevated PTH levels are caused by the prolonged elevation of thyrotropin (TSH) levels (*i.e.* [Paloyan et al](#), 1997). **Fluoride is a TSH analogue.** *item...*

2002 - As a result of research into molecular biology ("the art of cloning") there are now hundreds upon hundreds of studies available documenting the actions of fluorides on cell proteins, the "On" and "Off" switches involved in cellular signal transmission.

During the 1980s and 1990s fluorides become known as the universal G-protein activator. Although there have been numerous studies before showing that fluorides act like thyroid-stimulating-hormone - as seen above -, it can now be documented in detail for it is known that G proteins in thyroid physiology are normally absolutely dependent on TSH and are inactive without it. TSH is the master, sometimes also referred to as the "violinist in the orchestra".

The TSH receptor is the only receptor known able to activate all G protein family members. Its activity directly imitated by fluoride.

see also: [Tables](#)

[Hyperparathyroidism](#)

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Treatment of thyroid disease by radioiodine

Candidates for radioiodine therapy:

1. Graves' disease (diffuse toxic goiter) with or without
ophthalmopathy

Radiotracer involving with therapy:

A. Iodine-130: It delivered more radiation to the apex of follicular cell.

B. Iodine-131: I-131 delivers about 70% of its radiation dose to thyroid gland and only 10% of its radiation exposes to the ovaries and testes.

C. Iodine -125: It has been evaluated for radiation therapy of hyperthyroidism but there is no evidence regarding advantage of I-125 over I-131.

Recently the population of hyperthyroid candidate has been extended to young adults, teenage or even young children.

In women of childbearing age, it is necessary to prove that the

pregnancy test is negative and to advise the patient not to get

pregnant after 6 months after therapy. Also breast feeding should

be discontinued about 2 weeks after therapy.

Advantages of I-131 for treatment of hyperthyroidism (Graves' disease)

a. I-131 emits beta particles that deposit 90% of their radiation

energy within an area of less than 1 mm from the decaying radiation

atom.

b. Physical half life of 8 days makes it easy, safe and simple.

c. It can be given outpatients

d. The radiation delivered by I-131 is efficiently penetrating to

overcome limitation related to the heterogeneity of radioiodine

concentration within the hyperfunctioning thyroid gland.

e. I-131 emits gamma photon that can be measured by external

radiation detectors.

f. Usually one dose is sufficient.

Disadvantages of I-131 therapy in graves' disease

a. Slow in action

b. Recovery from hyperthyroidism starts after 10-12 weeks

2. Plummer's disease (toxic nodular goiter)

A. Solitary toxic nodule

Radioiodine therapy has been successful in thyrotoxicosis produced

by a single thyroid nodule however, higher dose and more than

one dose are needed. After the treatment the nodule become smaller

but not disappeared.

B. Toxic multinodular goiter

In treatment of multinodular goiter by I-131 also higher doses is

recommended. Multinodular goiter is more resistant to therapy

due to nonhomogeneity. Since different region of those huge glands have different degree of hyperfunction. It seems that the

enlargement is persist even after the hypothyroidism has been

treated . Therefore in cases with large toxic goiters thyroidectomy

may be recommended.

3. Thyroid carcinoma and metastases

Among patients with thyroid cancer, those with the well differentiated thyroid carcinoma (papillary CA and follicular CA) are candidate for radioiodine therapy (I-131) after thyroidectomy and lymph node resection because Well differentiated neoplasm have the ability to accumulate radioiodine.