

Environmental Exposures and Autoimmune Thyroid Disease

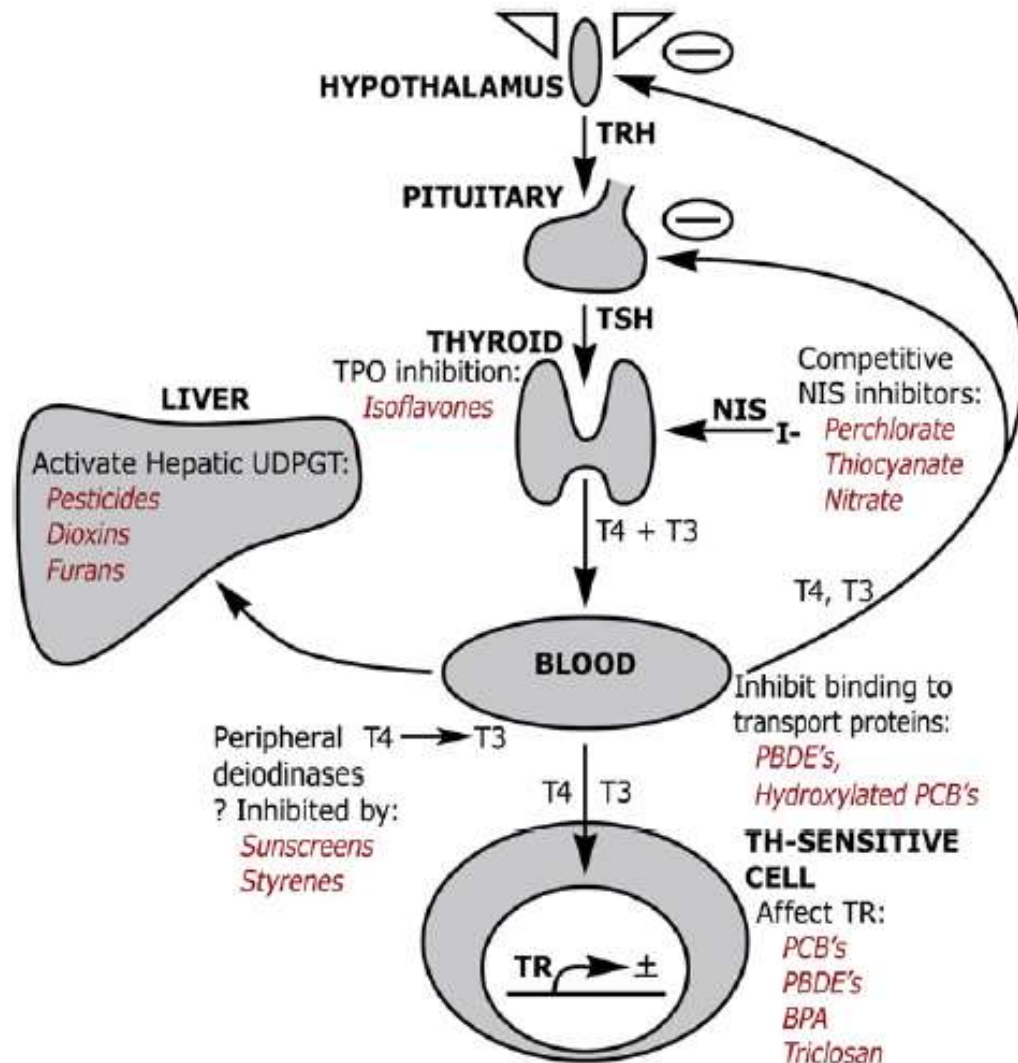
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Etiologies of Hypothyroidism

- Chronic autoimmune thyroiditis-Hashimoto's disease
- Partial thyroidectomy.
- Radioactive iodine therapy for treatment of hyperthyroidism.
- External radiotherapy of the head and neck in patients with Hodgkin's lymphoma, leukemia, brain tumors, or bone-marrow transplantation.
- Infiltrative disorders of the thyroid gland (eg, amyloidosis, sarcoidosis, hemochromatosis, or Riedel's thyroiditis).

Pathways of Environmental Agent Thyroid Disruption



Environmental Agents That Interfere With Thyroid Function

Agent	Example of Sources	Mode of Action	Thyroid Disease in Humans
Polychlorinated biphenyls (PCBs)	Found in coolants and lubricants, properties; multiple congeners, lipophilic	TR agonist/antagonist, can alter levels of T4 and TSH	Possible increase in TSH, thyroid autoantibodies, thyroid volume
Organochlorine pesticides	Used as pesticide on crops	Induce hepatic glucuronyltransferase (UDPGTs)	No established association
Polybrominated diphenylethers (PBDEs)	Found in flame retardants	Bind to TRs, displaces T4 from binding proteins	Increase in hypothyroidism in some studies
Bisphenol-A (BPA)	Used in plastic bottles	Antagonize TR, lower serum T4	No established association

Adapted from Brent GA Thyroid 20:755, 2010

Environmental Agents That Interfere With Thyroid Function

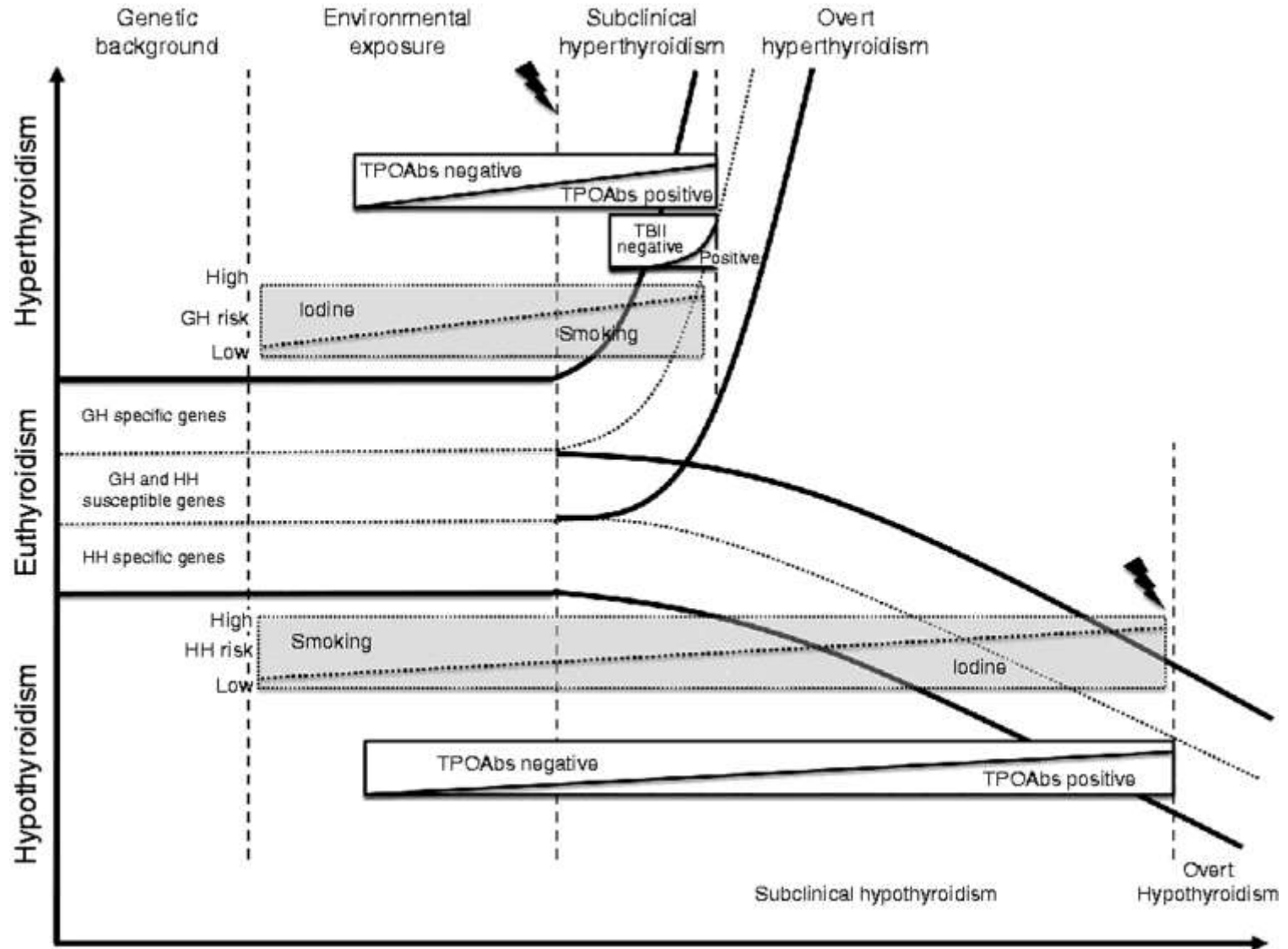
Agent	Example of Sources	Mode of Action	Thyroid Disease In Humans
Perchlorate, Thiocyanate	Rocket fuel, fertilizer, smoking	Inhibits iodine uptake, at sufficient levels reduces T4	No established association
Triclosan	Antibacterial in soaps	Reduces serum T4, disrupts amphibian development	No established association
Isoflavones	Soy products	Inhibits TPO activity	Possible increase in hypothyroidism

Adapted from Brent GA Thyroid 20:755, 2010

“Triggers” of Autoimmune Thyroid Disease

- Stress (?)
- Smoking
- Estrogen
- Pregnancy/Postpartum
- Existing Thyroid Autoantibodies/Genetic Risk
- Drugs-eg. Amiodarone, Lithium, cytokines (IL-2, interferon alpha)
- Iodine/Selenium status
- Viral and bacterial infections
- Environmental toxicants
- Medical radiation
- Environmental radiation exposure
- Iodine excess

Proposed Model for the Natural History of AITD



GH-Graves' hyperthyroidism

Effraimidis G et al. Eur J Endocrinol 164:107, 2011

HH-Hashimoto's hypothyroidism

Population Urinary Iodine Values and Iodine Nutrition

Median Urinary Iodine Concentration (µg/L)	Corresponding Iodine Intake (µg/day)	Iodine Nutrition
<20	<30	Severe deficiency
20-49	30-74	Moderate deficiency
50-99	75-149	Mild deficiency
100-199	150-299	Optimal
200-299	300-449	More than adequate
>299	>449	Possible excess

Iodine-Containing Medications

Expectorants

[Iphen (25 mg/ml)]
[Par glycerol (5 mg/ml)]
[R-Gen (6 mg/ml)]

Antiasthmatic drugs

[Mudrane (195 mg/tab)]
[Iophylline (2 mg/ml)]
[Elixophyllin-K1 elixir (6.6 mg/ml)]

Antiarrhythmics

Amiodarone (75 mg/200 mg tab)

Antiamebics

Iodoquinol (134 mg/tab)

Douches

Povidone-iodine (10mg/ml)

Topical Antiseptics

Povidone-Iodine (10 mg/ml)
Clioquinol cream (12 mg/gm)

Radiographic Contrast Agents

[Iopanoic acid (333 mg/tab)]
[Ipodate sodium (308 mg/tab)]
IV preparations (140-380 mg/ml)
- Optiray 320mg/ml (CT scans)
- Visipaque 150, 270, or 320 mg/ml
(coronary angiography)

Iodides

SSKI (25 mg/drop)
Lugol's solution (5 mg/drop)

Adapted from M. Surks Up-to-Date

Iodine Induction of Autoimmunity

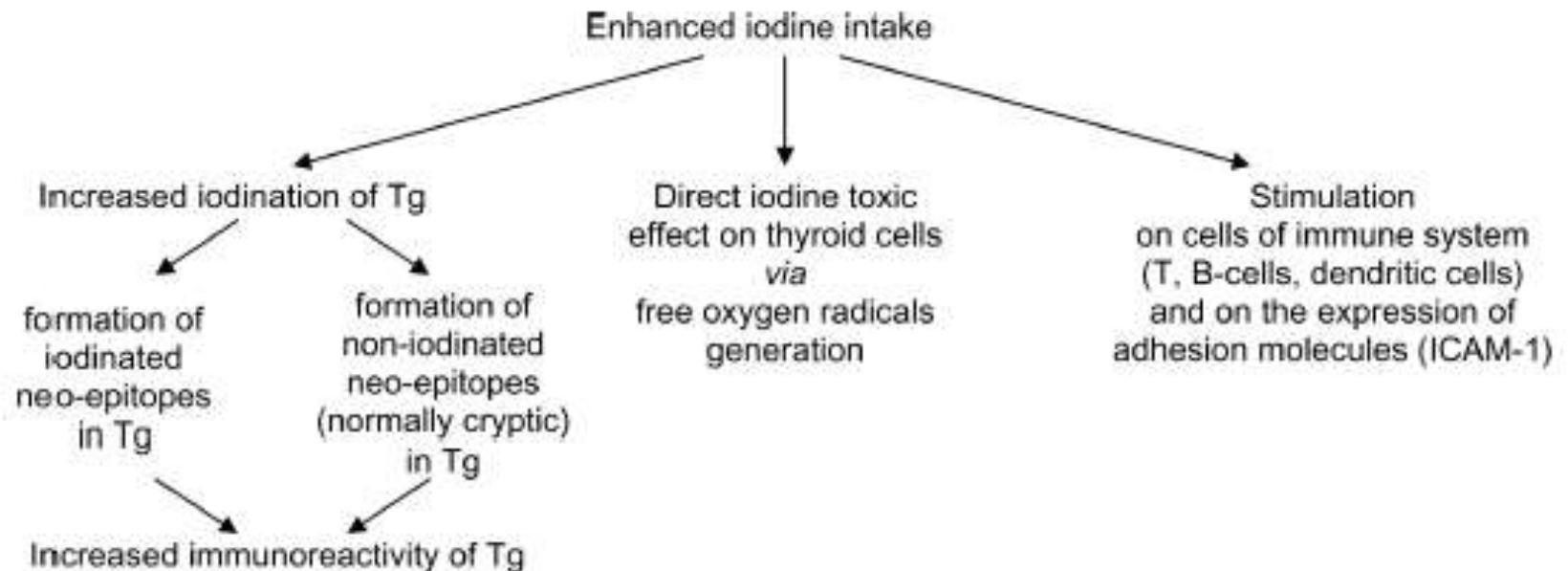


FIG. 1. Suggested mechanisms inducing iodine thyroid autoimmunity.

Medical Radiation

- Stimulation of antithyroid antibodies and autoimmune thyroid disease with external radiation for Hodgkin's disease.
- Thyroid hypofunction most common, but hyperthyroidism also seen.
- Reports of Graves' hyperthyroidism and ophthalmopathy after radioiodine for thyroid autonomy.

Susceptible Populations

- Lower Socioeconomic Status-Higher exposure to environmental toxicants.
- Radiation Exposed-Medical and Environmental.
- Reduced ability to “compensate” for impairment of thyroid hormone axis: fetus, infant, pregnancy women, iodine deficient, partial thyroidectomy, thyroid autoantibodies.
- Smoking

Risk Reduction of in the Individual Patient

Susceptibility Factor	Mechanism	Reduce or Monitor Risk
Genetic Background Family History of Thyroid Disease	Increase genetic susceptibility to environmental triggers.	Awareness/avoidance of triggers Low clinical threshold for thyroid function testing.
Excess Dietary Iodine	Increased immunogenicity of thyroglobulin, thyroid cell destruction.	Maintain regular and sufficient intake, especially during pregnancy.
Dietary Goitrogens eg. cassava, cabbage, soy(?)	Interfere with iodine uptake, thyroid hormone synthesis	Sufficient iodine intake markedly reduces susceptibility.
Cigarette Smoking	May increase cytokines in orbit and thyroid, complex interactions with the immune system.	Increased risk of Graves' disease and Graves' ophthalmopathy Reduced risk of Hashimoto's disease.

Adapted from Brent GA Thyroid 20:755, 2010

Risk Reduction in the Individual Patient (continued)

Susceptibility Factor	Mechanism	Reduce or Monitor Risk
Nuclear Incident	Direct thyroid destruction, increased thyroid antigens	Potassium iodine ingestion at time of incident.
Medications	Stimulation of immune response at multiple sites.	Thyroid function tests and thyroid autoantibodies in susceptible individuals, thyroid function test monitoring.
Environmental Toxicants/Chemicals	Promotes autoimmune thyroiditis in susceptible animal models.	Monitoring thyroid function tests and thyroid autoantibodies, test well water for contaminants.
Medical Radiation	Increase thyroid antigens, inflammation.	Awareness of increased incidence of Hashimoto's and Graves' disease, thyroid function test monitoring.