Recent Topics in Thyroid Pharmacology

Mohammed Sayed, PhD.
Vice-Chair and Assistant Professor of Pharmacology
DeBusk College of Osteopathic Medicine
Lincoln Memorial University

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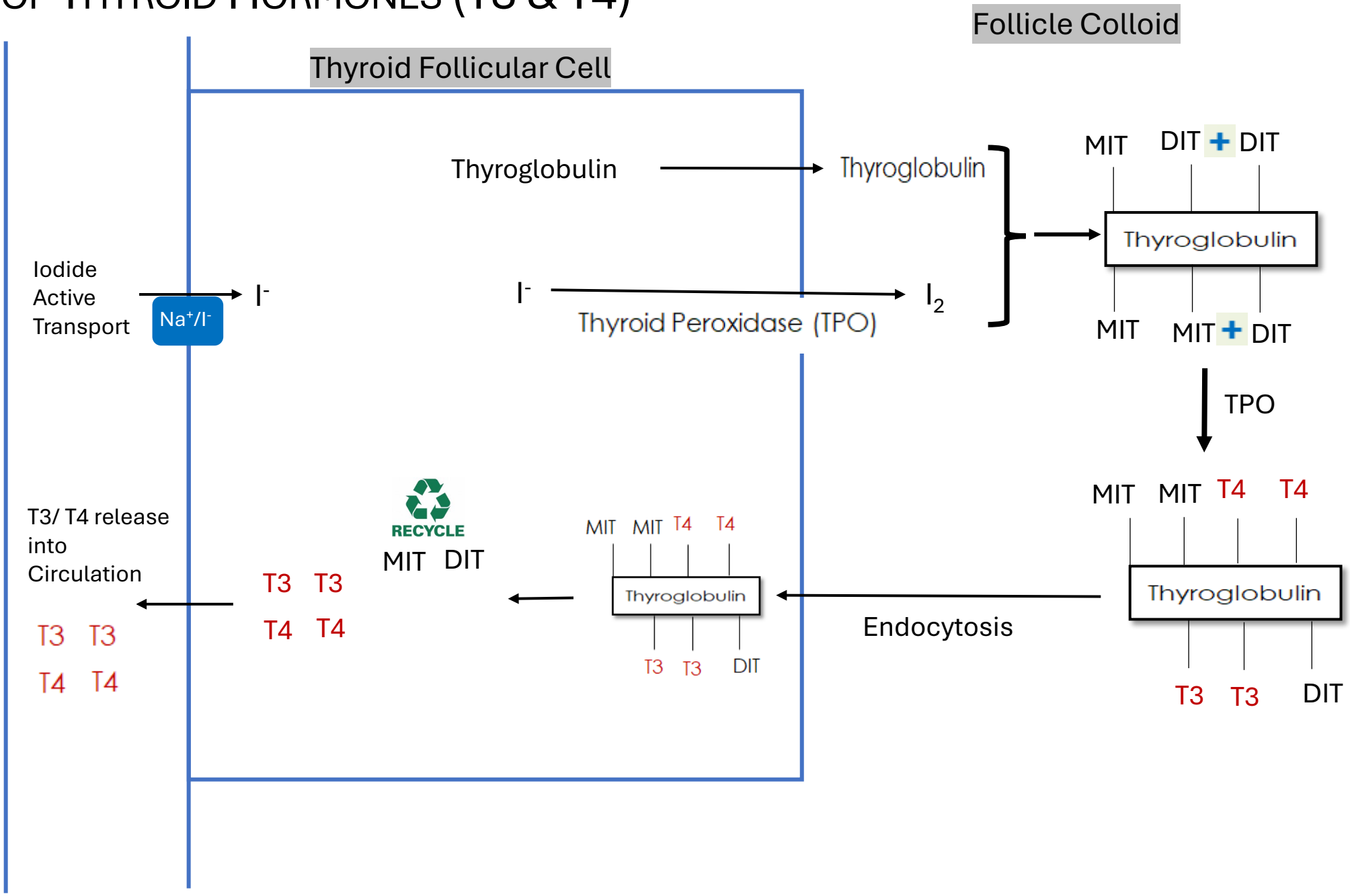
Disclosures

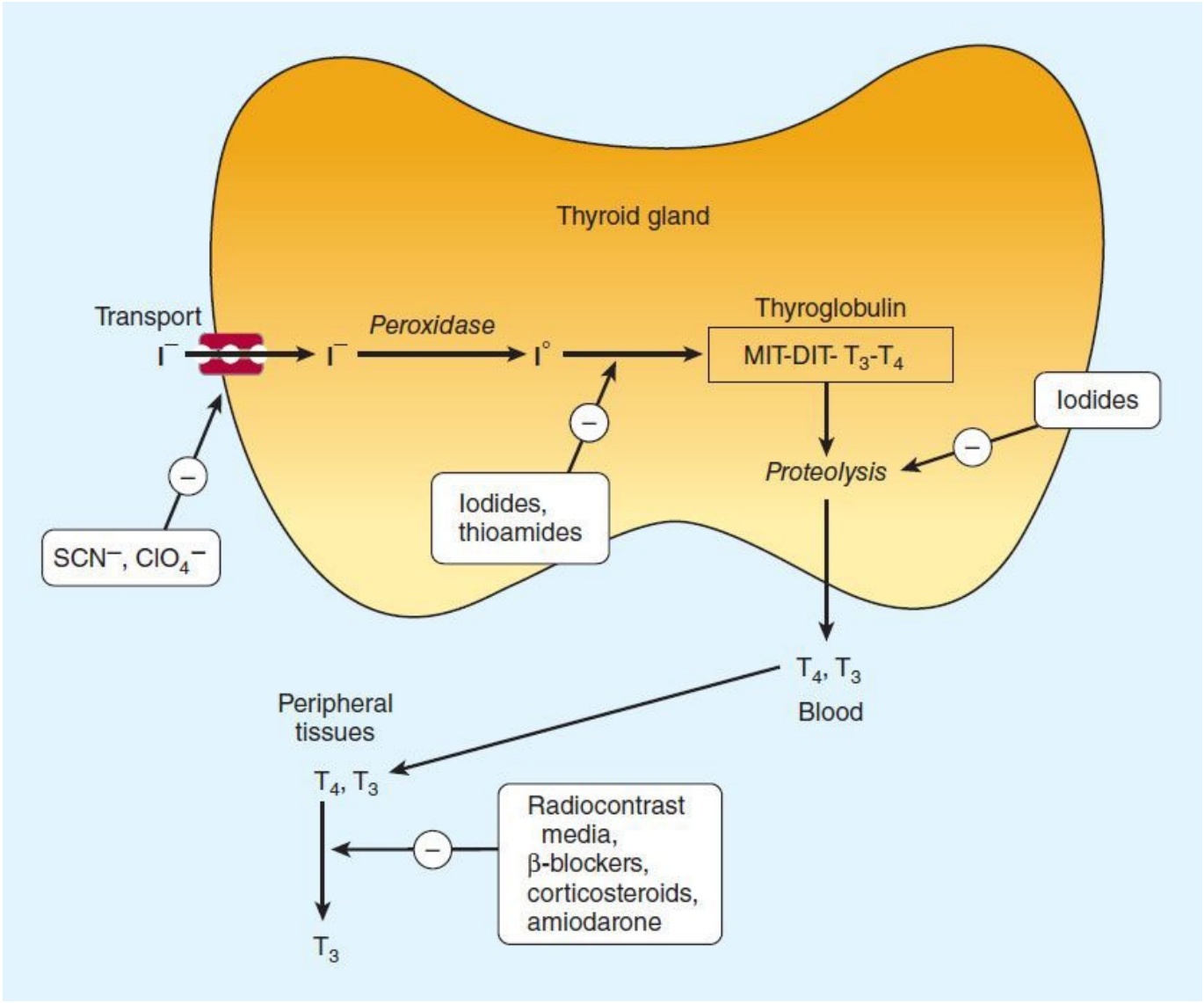
I have no financial relations/conflicts of interests to disclose.

Objectives

- The learner will review the biochemical pathway of thyroid hormone production and the major targets for antithyroid drug action.
- The learner will learn to assess the need of iodine supplementation in pregnant females and decide whether to prescribe iodine supplements according to the 2026 ATA guidelines.
- The learner will learn to identify the risk-factors associated with the use of antithyroid drugs (ATDs) in pregnancy and to select the appropriate ATD treatment according to the 2026 ATA guidelines.
- The learner will learn the appropriate usage of radioactive iodine (RAI) therapy in treating differentiated thyroid cancer (DTC).
- The learner will be able to counsel patients regarding some of the major safety considerations with RAI therapy.

SYNTHESIS OF THYROID HORMONES (T3 & T4)





Biosynthesis of thyroid hormones.

The sites of action of various drugs that interfere with thyroid hormone biosynthesis are shown.

Adapted from:
https://basicmedicalkey.com/thyroid-antithyroid-drugs/

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Thyroid Pharmacology in Pregnancy

American Thyroid Association 2026 Guidelines for Thyroid Disease in Preconception, Pregnancy, and Postpartum [1]

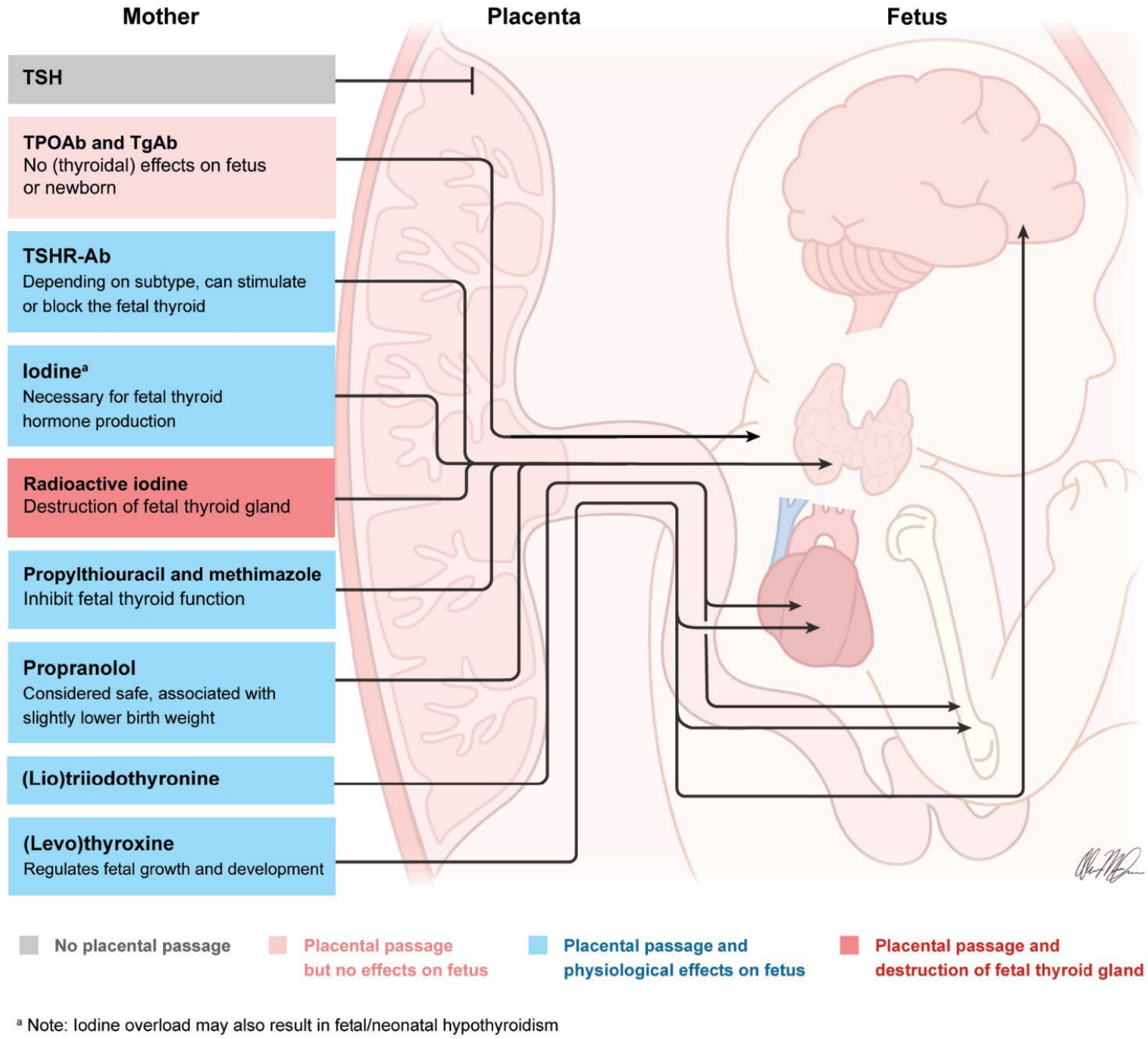

FIG. 2. **Transplacental passage of thyroid parameters and drugs.**

Maternal TSHR-Ab, iodine, radioactive iodine, the antithyroid drugs (propylthiouracil and methimazole), propanolol, and the thyroid hormones [(lio)thyronine and (levo)thyroxine] all traverse the placenta and have the potential to induce direct effects to the fetus. Maternal TPOAb and TgAb can also traverse the placenta but do not affect the fetus. Maternal TSH does not cross the placenta. TPOAb, thyroperoxidase antibody; TgAb, thyroglobulin antibody; TSHR-Ab, thyrotropin receptor antibody. [1]

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Iodine Nutrition in Pregnancy

American Thyroid Association 2026 Guidelines for Thyroid Disease in Preconception, Pregnancy, and Postpartum [1]

Recommendations Table 3: Iodine Nutrition	Strength*	Level #
Pregnant and lactating women should strive for a daily iodine intake of 250 mcg as provided by dietary iodine intake complemented by iodine supplements as required.	Strong	Moderate
For women at risk of iodine deficiency given geographic region, dietary restrictions or malabsorption, we suggest starting 150 mcg per day iodine supplementation ideally at least 3 months before planned pregnancy and continued until lactation is complete.	Conditional	Moderate
An annual dose of 400 mg iodized oil in women of childbearing age and pregnant women can be given in low-resource countries and/or regions with severe iodine deficiency, where neither salt iodization nor daily iodine supplements are feasible.	Conditional	Moderate
We suggest applying similar iodine supplementation recommendations for pregnant women taking antithyroid drugs (ATDs) for Graves' hyperthyroidism and those taking levothyroxine for hypothyroidism.	Conditional	Low
Excessive iodine exposure during pregnancy should be avoided with the exception of certain medical indications, such as the use of saturated solution of potassium iodide (SSKI) or iodinated contrast media.	Strong	Moderate
Sustained excessive dietary iodine intake and dietary supplements use exceeding 500 mcg daily should be avoided during pregnancy due to concerns for fetal and maternal thyroid dysfunction.	Strong	Moderate

* Strength of Recommendation; # Level of Evidence; Good Practice Statement
ATD, antithyroid drug; SSKI, saturated solution of potassium iodide

What is new in the 2026 guidelines:

- There remains no valid biomarker for measuring long-term iodine status in an individual person (currently available biomarkers, including urinary iodine concentrations [UICs], are intended only to be interpreted as median levels in populations).

- Risk factors for iodine deficiency on the individual level should continue to be considered when applicable.

Antithyroid Drugs (ATDs) in Pregnancy

American Thyroid Association 2026 Guidelines for Thyroid Disease in Preconception, Pregnancy, and Postpartum [1]

Prevalence of congenital malformations			
Unexposed ATD group	PTU use only	MMI/CMZ use only	Both PTU and MMI/CMZ
	Within 1 year of birth[a]		
5.9% **(N=170,716/2,872,109)**	7.0% (N=699/9,930)	8.1% (N=91/1,120)	8.0% (N=147/1,841)
	Within 2 years of birth[b]		
5.7% **(N=45,982/811,730)**	8.0% (N=45/564)	9.1% (N=100/1,097)	10.1% (N=16/159)

[a] Seo GH, et al. Ann Intern Med 2018;168(6):405-413.
[b] Andersen SL, et al. J Clin Endocrinol Metab 2019;104(12):6040-6048.

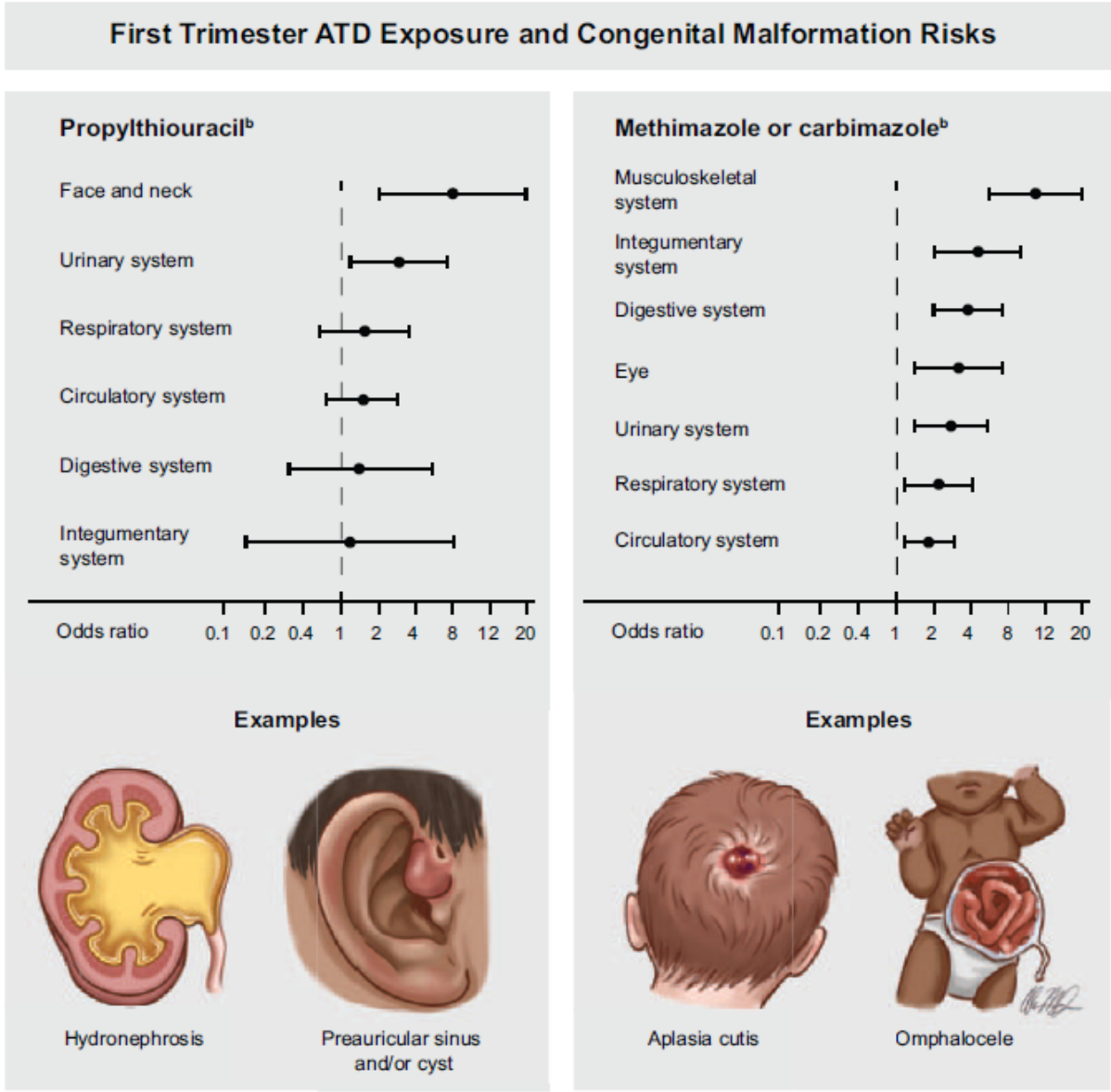


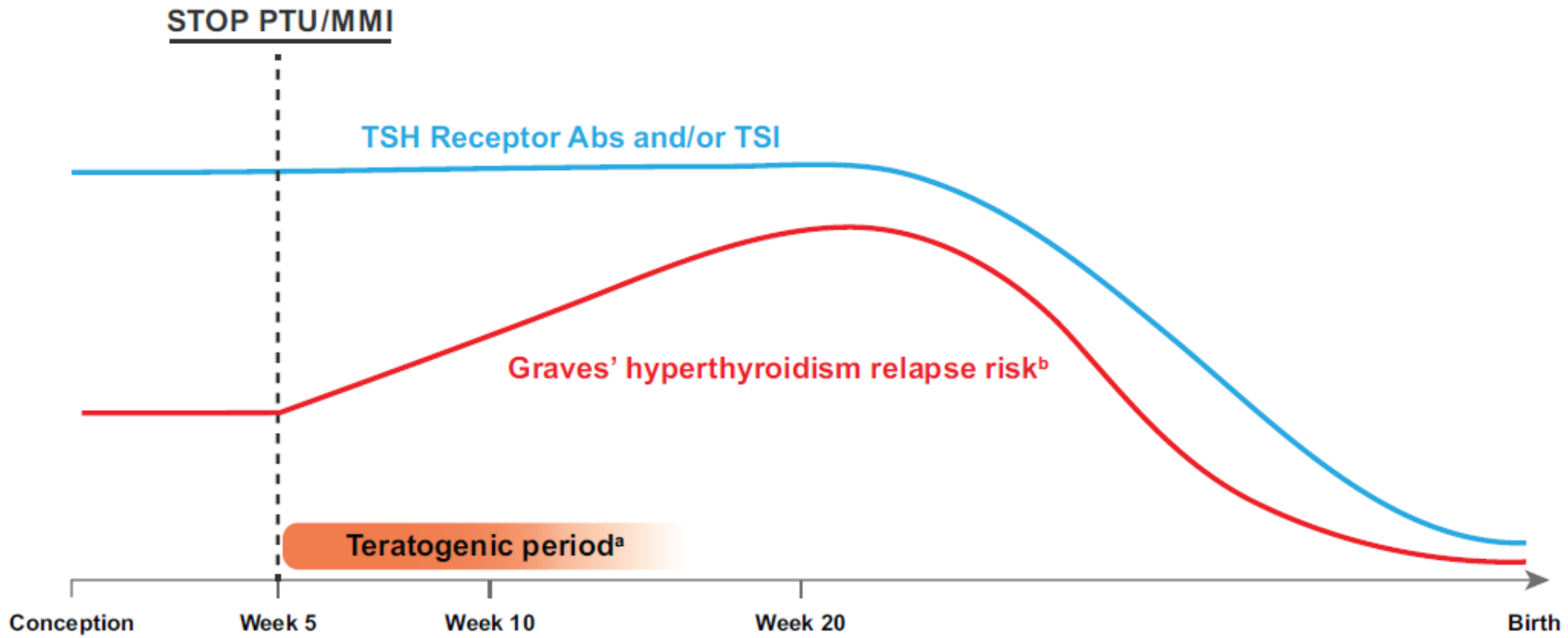
FIG. 6. Risks of antithyroid drugs during pregnancy. The relative and absolute risks, as well as examples of affected
organ systems and severity of congenital malformations, associated with maternal antithyroid drug use during pregnancy
are summarized from data reported in two large epidemiological studies. CMZ, carbimazole; MMI, methimazole. [1]

Preconception management of hyperthyroidism (Graves' disease)

Recommendations Table 14: Graves' Disease Preconception	Strength*	Level #
The desire for conception should be assessed in women of childbearing age who have new or existing hyperthyroidism.	Good Practice Statement	
The risks and benefits of treatment options for hyperthyroidism, their impacts on a future pregnancy, and desired timeline to conception should be discussed in women with existing hyperthyroidism who are planning pregnancy.	Good Practice Statement	
Women taking methimazole (MMI) should be switched to propylthiouracil (PTU) if they are planning pregnancy.[a]	Strong	Moderate

[a] If PTU is not available or if there are contraindications (allergy), we recommend that women continue MMI while trying to conceive, along with a discussion on the pros and cons of stopping MMI upon a positive pregnancy test and the option to pursue definitive therapy prior to pregnancy.
* Strength of Recommendation; # Level of Evidence; Good Practice Statement
MMI, methimazole; PTU, propylthiouracil

Graves' disease treatment option	Risks	Guidance
ATDs	Congenital anomalies (more severe with MMI than PTU)	• Discuss ATD risks in pregnancy through shared decision-making in preconception. • Confirm pregnancy promptly if suspected. • Consider discontinuing ATDs in pregnant women at low risk of disease relapse during the first trimester. • If PTU is available, consider switching from MMI to PTU as soon as pregnancy is confirmed, using a dosing ratio of 1:20 (MMI to PTU). • If ATD use continues to be needed during pregnancy, treat with PTU (if available) until 16 weeks gestation. The choice for a preferred ATD after 16 weeks gestation is unknown.
	Fetal goiter	• Monitor maternal thyroid function every 2-4 weeks, aiming for FT4 concentration at or slightly above the upper third of the reference interval. • Fetal ultrasound monitoring should be performed monthly starting at 18-20 weeks gestation if the mother uses ATDs during pregnancy, monitoring frequency can be reduced for low dose ATD on a case-by-case basis. • If ATDs can be discontinued in pregnancy, then the maternal TRAb and/or TSI concentration can be checked[a] and subsequent fetal ultrasound follow-up can be continued if the result remains >3 times the upper limit of normal after approximately 18-20 weeks gestation.
	Fetal and neonatal thyroid dysfunction	• Same guidance as for "Fetal goiter" above. • Consider discontinuing ATD treatment by 30-34 weeks gestation if appropriate.



[a] For MMI/CMZ, the teratogenic period ends at approximately 16 weeks for skin defects, while the risks for other congenital anomalies remain elevated generally throughout the first trimester.
[b] The 1 year risk of Graves' disease relapse typically ranges between 30-70% following ATD discontinuation based on risk factors in the text.
ATD, antithyroid drug; TSHR-Ab, thyrotropin receptor antibody; TSI, thyroid stimulating immunoglobulin

FIG. 5. Strategy for ATD discontinuation upon pregnancy confirmation. Factors important for considering when maternal ATD may be successfully discontinued in pregnancy include the duration and dose of ATD use, maternal TSH concentration, signs of Graves' disease burden (i.e., thyroid eye disease, goiter), and the maternal TRAb and/or TSI concentration. The 1-year risk of Graves' disease relapse typically ranges between 30% and 70% following ATD discontinuation based on these risk factors.

ATD treatment of Graves' disease in preconception and pregnancy

Recommendations Table 17: ATD Treatment of Graves' Disease Preconception and in Pregnancy	Strength*	Level #
Consider discontinuing ATD therapy for Graves' disease upon confirmed pregnancy if the woman is euthyroid on low dose ATD (MMI <5–10 mg/day or PTU <100–200 mg/day) taken for >6 months pre-pregnancy (Figure 4).	Conditional	Low
Following the discontinuation of ATD use in pregnancy, serum TSH, FT4 and clinical examination may be monitored every 1-2 weeks in the first trimester, then every 2-4 weeks in the second and third trimesters.	Conditional	Low
In pregnant women with a new diagnosis of Graves' hyperthyroidism or who have high risk of developing thyrotoxicosis if ATDs were to be discontinued, treatment with ATDs is advised as follows:		
Pregnant women with active Graves' disease managed with ATDs should have serum TSH, FT4, and TRAb and/or TSI concentrations measured as soon as pregnancy is confirmed and monitored with TSH and FT4 every 2-4 weeks thereafter.	Good Practice Statement	
PTU may be used if initiating ATD for the treatment of hyperthyroidism before 16 weeks of pregnancy.	Conditional	Low
If a woman is taking MMI during pregnancy, switching to PTU[a] may be considered until 16 weeks[b] depending on the time of presentation and MMI dose (see text).	Good Practice Statement	
If PTU is not available, MMI may be continued at the lowest effective dose for the shortest duration possible.	Conditional	Low
In case of thyrotoxicosis, propranolol may be used in routine dosages to ameliorate hyperthyroidism-related symptoms.	Good Practice Statement	

[a] When switching from MMI to PTU, a dose ratio of approximately 1:20 should be used (e.g., MMI 5mg once daily = PTU 50mg twice daily).
[b] If ATD therapy continues to be required after 16 weeks gestation, it remains unclear whether PTU should be continued or switched to MMI.
* Strength of Recommendation; # Level of Evidence; Good Practice Statement
ATD, antithyroid drug; MMI, methimazole; PTU, propylthiouracil; TSH, thyroid stimulating hormone; FT4, free thyroxine; TRAb, TSH receptor antibodies; TSI, thyroid stimulating immunoglobulin

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Radioactive Iodine (RAI) Use in Differentiated Thyroid Cancer (DTC)

2025 American Thyroid Association Management Guidelines for Adult Patients with Differentiated Thyroid Cancer [2]

Important Definitions

- **Remnant ablation**: Eliminate residual benign thyroid tissue in the thyroid bed to facilitate treatment monitoring.
- **Adjuvant therapy**: Additional RAI administered to reduce the risk of recurrence.
- **Treatment of known disease**: Treatment of known areas of residual/metastatic disease.

What is the role of RAI after thyroidectomy in the primary management of DTC?

A. Remnant ablation is not recommended routinely after total thyroidectomy for patients with ATA low-risk DTC. (Strong recommendation, High certainty evidence)

B. RAI adjuvant therapy may be considered after total thyroidectomy in patients with ATA low-intermediate and intermediate-high risk of recurrent DTC. (Conditional recommendation, Low certainty evidence)

What is the role of RAI after thyroidectomy in the primary management of DTC? (cont.)

C. RAI adjuvant therapy is recommended routinely after total thyroidectomy for patients with ATA high-risk DTC. (Strong recommendation, Moderate certainty evidence)

D. In patients with an initial diagnosis of DTC with distant metastases, RAI therapy is recommended routinely after total thyroidectomy. (Strong recommendation, Moderate certainty evidence)

TABLE 10. SUMMARY OF RECOMMENDATIONS FOR INITIAL RAI FOLLOWING THYROIDECTOMY[a]

Risk category	*Typical RAI recommendation*	*Recommended ^{131}I activity level*	*Goals of therapy*
Low	No	1.1–1.85 GBq (30–50 mCi)	None or remnant ablation
Intermediate-low and intermediate-high	Consider	1.1–3.7 GBq (30–100 mCi)	Remnant ablation +/– adjuvant therapy
High	Yes	3.7–5.55 GBq (100–150 mCi)	Remnant ablation and adjuvant therapy
Distant metastases	Yes	3.7–7.4 GBq (100–200 mCi) or consider dosimetry	Treatment of known disease, remnant ablation

[a]Note that these recommendations represent guidelines and that a variety of additional features including patient preference, comorbid conditions, access to care, pre-therapy imaging, and others may influence the decision to treat with RAI as well as the resulting activity level. Consistent with the Martinique documents, the final recommendation for administered activity should be based on multidisciplinary management recommendations.[760]

RAI, radioactive iodine.

Should a low-iodine diet be prescribed prior to RAI administration?

A low-iodine diet for approximately 1–2 weeks should be used for patients undergoing RAI remnant ablation or treatment. (Good Practice Statement)

- (A low-iodine diet is generally defined as a restriction in iodine consumption to <50 mcg/day.)
- There are currently no randomized controlled trials that assess the impact of a low-iodine diet on the efficacy of RAI for any of its uses, limiting the strength of this recommendation.

How do you counsel and minimize risks of RAI side effects to the salivary glands and lacrimal ducts?

A. Patients should be counseled that RAI treatment may be associated with (acute and chronic) salivary gland morbidity, lacrimal duct stenosis, and potential risk of secondary malignancies. (Good Practice Statement)
B. For prevention of salivary gland side effects after RAI, general measures including hydration are recommended. (Good Practice Statement)
C. Patients with xerostomia are at increased risk of dental caries and should discuss preventive strategies with their dental health professional. (Good Practice Statement)

How should patients be counseled regarding the risk of second primary malignancy after receiving RAI therapy?

Patients should be counseled about the risks of second primary malignancy (SPM) after RAI treatment for DTC. The absolute increase in risk attributable to RAI appears to be small and does not warrant additional screening for SPM. (Good Practice Statement)

How should patients be counseled about RAI therapy and pregnancy, nursing, and gonadal function?

A. Female patients of reproductive age receiving RAI therapy should have a negative screening evaluation for pregnancy prior to RAI administration and avoid pregnancy for at least 6 months after receiving RAI. (Good Practice Statement)

B. RAI should not be given to nursing female patients. Depending on the clinical situation, RAI therapy should be deferred until lactating women have stopped breast-feeding or pumping for at least 3 months. A diagnostic ^{123}I scan may be performed in recently lactating women to detect breast uptake that may warrant deferral of therapy. (Good Practice Statement)

How should patients be counseled about RAI therapy and pregnancy, nursing, and gonadal function? (Cont.)

C. Male patients receiving cumulative radioiodine activities >14.8 GBq (400 mCi) should be counseled regarding potential risks of infertility. (Good Practice Statement)

D. Female patients receiving RAI should be counseled that such therapy has not been shown to impact future fertility. (Good Practice Statement)

References

[1] Korevaar TIM, Leung AM, Alexander EK, et al. American Thyroid Association 2026 Guidelines for Thyroid Disease in Preconception, Pregnancy, and Postpartum. *Thyroid*. 2026;36(5):481-544. doi:10.1177/10507256261445624

[2] Ringel MD, Sosa JA, Baloch Z, et al. 2025 American Thyroid Association Management Guidelines for Adult Patients with Differentiated Thyroid Cancer. *Thyroid*. 2025;35(8):841-985. doi:10.1177/10507256251363120