

THYROID FUNCTION ASSESSMENT & MONITORING IN WOMEN OF CHILD-BEARING AGE

This Calgary Zone best-practice clinical pathway has been developed with consideration of guidelines. It includes a flow diagram and expanded details.

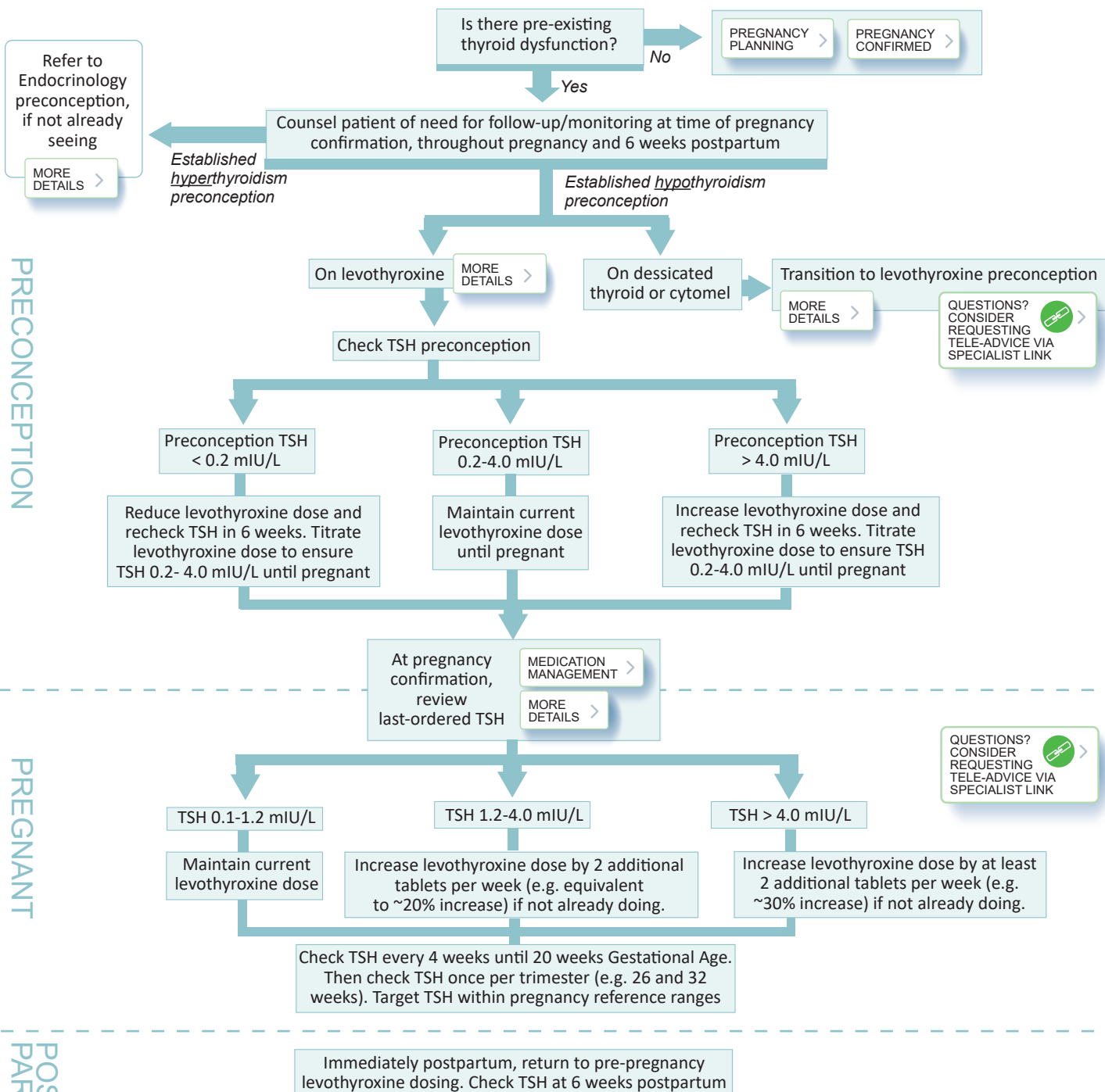
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CLINICAL FLOW DIAGRAM



Focused summary of thyroid function assessment and monitoring in women of child-bearing age in primary care

No pre-existing thyroid disease and pregnancy planning

Routine screening for thyroid disease is not currently justified during the pregnancy planning period. Only if there are symptoms and signs of hypo or hyperthyroidism or risk factors such as other autoimmune disease (i.e. type 1 diabetes, celiac etc.), a Thyroid Stimulating Hormone level (TSH) may be helpful.

No pre-existing thyroid disease and pregnancy confirmed

Despite recent practice, routine testing of TSH during prenatal screening is not currently justified. There is no evidence of benefit of levothyroxine therapy for subclinical hypothyroidism on obstetrical, neonatal, childhood IQ or neurodevelopmental outcomes¹. Routine thyroid testing during pregnancy frequently leads to initiation of thyroid medication for minor test result abnormalities, which would have spontaneously normalized without intervention. Excessive testing has resulted in unnecessary healthcare spending and potential harm to women and their children.

If a TSH is ordered during pregnancy because of symptoms and signs of hypo or hyperthyroidism or risk factors such as other autoimmune disease:

1. If TSH <0.1 mIU/L, check FT4 and FT3. If FT4 and or FT3 are elevated, consider referral to Endocrinology CAT or call Specialist Link for advice.
2. If TSH 0.1-5.0 mIU/L, no further intervention or lab testing is required
3. If TSH 5.1-10.0 mIU/L, repeat TSH in 2 weeks; if repeat testing is still 5.1-10.0 mIU/L, consider trajectory of change over 2 weeks and call Specialist Link for assistance if required. If decision to start levothyroxine is made use low dose i.e. 50 mcg/day). If levothyroxine initiated during pregnancy stop postpartum and recheck TSH 6 to 12 weeks postpartum.
4. If TSH >10.0 mIU/L, start levothyroxine 2.0 mcg/kg and follow established hypothyroidism algorithm for care.

Established pre-existing thyroid disease and pregnancy planning

For women with a known history of thyroid disease, a TSH is important to ensure that they are euthyroid prior to conception. Counsel patients with pre-existing thyroid disease, that during the childbearing years, they may require more frequent testing and medication adjustment. See attached algorithm for management during pregnancy.

Checklist to guide your in-clinic assessment and management of thyroid function in the female patient planning pregnancy or during the prenatal period

- ☐ Routine screening with a TSH or other thyroid investigations is NOT INDICATED in asymptomatic women without a history of thyroid dysfunction and without signs or symptoms of thyroid dysfunction.
- ☐ If clinical assessment of patient is consistent with hypo or hyperthyroidism, TSH may be ordered to help guide management.
- ☐ If pre-existing HYPOTHYROIDISM, ensure euthyroid prior to and at time of conception; monitor TSH at time of pregnancy confirmation and every 4 weeks less than 20 weeks gestation or until stable TSH is achieved; adjust levothyroxine to achieve and maintain a TSH within gestational age specific reference ranges; postpartum, resume pre-pregnancy levothyroxine dose and check TSH at 6 weeks to ensure it is in the normal range.
- ☐ If pre-existing HYPERTHYROIDISM, refer to Endocrinology pre-conception for careful consideration of treatment options.

Expanded Detail

Established pre-existing hypothyroidism:

- 1. Preconception or pregnant:** Women with pre-existing hypothyroidism should be advised to avoid ingesting levothyroxine with iron or calcium containing supplements (including those found in prenatal vitamins); Ingestion should be separated by at least 4 hours. Co-ingestion has been shown to interfere with the absorption of thyroid hormone.
- 2. Preconception or pregnant:** Women on other thyroid preparations such as triiodothyronine (T3) (Cytomel) or desiccated thyroid should be switched to equivalent dose of levothyroxine as per table below (Table 1) and have repeat TSH (6 weeks later) to ensure euthyroid state prior to conception. Women using T3 or T3 and T4 combined preparations are likely at risk for having insufficient transfer of maternal T4 to the fetal brain. Other thyroid preparations such as triiodothyronine (T3) (Cytomel) or desiccated thyroid should not be used in pregnancy

TABLE 1: Product Dosage Equivalencies for converting to levothyroxine pre-conception / during pregnancy

Desiccated Thyroid Dose (mg)	Equivalent levothyroxine (L-T4) dose (mcg)	Equivalent Liothyronine (T3) (i.e. Cytomel) (mcg)
	50	10
60	88	
90	137	

120	175	
150	225	

3. **Preconception:** Women with established pre-existing hypothyroidism often require an increase in levothyroxine **once they are pregnant**. At pregnancy confirmation visit, review last TSH.
4. **Pregnant:** At pregnancy confirmation visit, review last TSH. Repeat TSH every 4 weeks until 20 weeks gestational age or until a stable normal range TSH is achieved). Check TSH once a trimester thereafter (e.g. 26 and 32 weeks gestation).

TABLE 2: Gestational Age Specific Reference Ranges on Calgary Lab Services Assay: for use in titrating levothyroxine during pregnancy in women with established hypothyroidism predating pregnancy

Weeks Gestation	TSH mIU/L
4 to 8	0.1 – 4.0
9 to 12	0.1 – 3.0
13 to 27	0.1 – 4.0
28 to term	0.5– 5.0

5. **Preconception:** Establish the **reason** patient is on levothyroxine (i.e. Thyroid cancer/ Grave's treated with RAI ablation or surgery). **Pregnant:** If history of Grave's, **TSH receptor antibody** (TRAB) must be checked by 20 weeks gestation. If positive (≥ 1.75), please call Endocrine through specialist LINK for further advice.
6. **Pregnant:** Women with pre-existing hypothyroidism often require an increase in the dose of levothyroxine once they are pregnant. This increase in dose can usually be achieved by taking two additional levothyroxine tablets per week which is equivalent to about a 20-30% increase in the total daily dose i.e. If taking levothyroxine 100 mcg/day prior to pregnancy, continue 100 mcg/day Monday to Friday and increase dose to 200 mcg on Saturday and Sunday or take levothyroxine 125 mcg daily.

Postpartum, women should return to their pre-pregnancy dose of levothyroxine. The TSH should be checked 6 weeks postpartum to ensure that it is normal.

Established pre-existing hyperthyroidism:

1. **Preconception:** Pregnancy planning should be delayed in women with active Grave's disease or toxic adenomas, until normal thyroid function is established. A referral to endocrinology needs to be made for all women with existing hyperthyroidism, as careful consideration of treatment options, maternal and fetal risks and benefits should be discussed with an Endocrinologist for all available therapeutic options (antithyroid drugs, radioactive iodine, thyroidectomy).
2. **Preconception:** Women who receive radioactive iodine require reliable contraception prior to radioactive iodine therapy and for at least **6 months after radioactive iodine**. A euthyroid state should be established prior to conception.
3. **Pregnant:** TSH, Free T4 and Free T3 should be checked at the time pregnancy is confirmed.

- 4. Pregnant:** If TSH is greater than 0.1 mIU/L and Free T4 and Free T3 normal and not on any antithyroid medication (i.e. Methimazole or PTU), there is usually no need for further follow up unless past history of I131 or thyroid surgery, in which case TSH receptor antibody (TRAB) should be checked and Endocrinology referral requested if positive (≥ 1.75).
- 5. Pregnant:** If patient is currently being treated for hyperthyroidism (e.g. patient taking Methimazole or PTU) OR TSH is less than 0.1 mIU/L, and Free T4 and/or Free T3 above trimester specific references (bit.ly/2BIWDIG) Table 3 refer to Endocrinology Central Access and Triage and consider calling Specialist Link for advice.

TABLE 3: Gestational Age Specific Reference Ranges, Calgary Lab Services

Weeks Gestation	Free T4 pmol/L	Free T3 pmol/L
4 to 8	10 – 25	3.5 – 6.5
9 to 12	11 – 22	3.5 – 6.0
13 to 27	10 – 19	3.5 – 6.0
28 to term	9.0 – 17	3.0 – 5.2

- 6. Pregnant:** If patient previously treated for Grave's with radioactive iodine or surgical resection of the gland (i.e. may now be on thyroid hormone replacement), check a TSH receptor antibody (TRAB) by 20 weeks gestation. If elevated (≥ 1.75) refer to Endocrinology Central Access and Triage and consider using Specialist LINK (specialistlink.ca) for tele-advice.

Physician/NP Resources

For Physicians
Division of Endocrinology – Thyroid Function in Pregnancy: bit.ly/2BIWDIG
Yamamoto et al BMJ Open 2018 Impact of levothyroxine on obstetric, neonatal and childhood outcomes in women with subclinical hypothyroidism diagnosed in pregnancy: a systematic review and meta-analysis of randomised controlled trials
Yamamoto JM and Donovan LE, Five Things to Know about Managing thyroid disease in women planning pregnancy CMAJ 2017, July 17;189 (28) E940

Patient Resources

For Patients
niddk.nih.gov/health-information/endocrine-diseases/pregnancy-thyroid-disease
Up To Date: Overview of thyroid disease and pregnancy (uptodate.com/contents/hyperthyroidism-overactive-thyroid-beyond-the-basics?search=hyperthyroidism%20in%20pregnancy&source=search_result&selectedTitle=1~13&usage_type=default&display_rank=1)

References

1. Yamamoto JM, Benham JL, Nerenberg KA, Donovan LE. Impact of levothyroxine therapy on obstetric, neonatal and childhood outcomes in women with subclinical hypothyroidism diagnosed in pregnancy: a systematic review and meta-analysis of randomized controlled trials *BMJ Open* 2018;**8**:e022837. doi: 10.1136/bmjopen-2018-022837
2. Yamamoto JM and Donovan LE, Five Things to Know about Managing thyroid disease in women planning pregnancy *CMAJ* 2017, July 17;189 (28) E940
3. Korevaar TI, Muetzel R, Medici M, *et al.* Association of maternal thyroid function during early pregnancy with offspring IQ and brain morphology in childhood: a population-based prospective cohort study. *Lancet Diabetes Endocrinol* 2016;**4**:35–43.
4. Medici M, Korevaar TI, Schalekamp-Timmermans S, *et al.* Maternal early-pregnancy thyroid function is associated with subsequent hypertensive disorders of pregnancy: the generation R study. *J Clin Endocrinol Metab* 2014;**99**:E2591–E2598.
5. León G, Murcia M, Rebagliato M, *et al.* Maternal thyroid dysfunction during gestation, preterm delivery, and birthweight. The Infancia y Medio Ambiente Cohort, Spain. *Paediatr Perinat Epidemiol* 2015;**29**:113–22.
6. Maraka S, Mwangi R, McCoy RG, *et al.* Thyroid hormone treatment among pregnant women with subclinical hypothyroidism: US national assessment. *BMJ* 2017;**356**:i6865.
7. Donovan LE, Metcalfe A, Chin A, Yamamoto JM, Virtanen H, Johnson JA, Krause R. A Practical Approach for the Verification and Determination of Site- and Trimester-Specific Reference Intervals for Thyroid Function Tests in Pregnancy. *Thyroid*. 2019 Mar;**29**(3):412-420. doi: 10.1089/thy.2018.0439
8. Haining Wang, Hongwei Gao, Hongbin Chi et al Effect of Levothyroxine on Miscarriage Among Women With Normal Thyroid Function and Thyroid Autoimmunity Undergoing In Vitro Fertilization and Embryo Transfer A Randomized Clinical Trial *JAMA*. 2017;**318**(22):2190-2198
9. Dhillon-Smith RK, Middleton LJ, Sunner KK et al Levothyroxine in Women with Thyroid Peroxidase Antibodies before Conception. *N Engl J Med*. 2019 Apr 4;**380**(14):1316-1325. doi: 10.1056/NEJMoa1812537. Epub 2019 Mar 23.

Disclaimer

This Calgary Zone Pathway has been developed with consideration of the most current evidence-based clinical guidelines from both Endocrinology and Primary Care literature for the assessment and management of thyroid function during the preconception and prenatal period.

This best-practice clinic pathway for the assessment, monitoring and management of thyroid function in the preconception and prenatal period in the primary care medical home. Included are flow diagrams and expanded detail explanation to guide this care.