Approved by Quality & Patient Care Committee
November 2016

THYROID DISEASE IN PREGNANCY

This LOP is developed to guide clinical practice at the Royal Hospital for Women. Individual patient circumstances may mean that practice diverges from this LOP.

1. AIM

- Appropriate management of a woman with subclinical or overt thyroid disease in pregnancy

2. PATIENT

- Woman with known or suspected thyroid disease in pregnancy

3. STAFF

- Medical and midwifery staff

4. EQUIPMENT

- Nil

5. CLINICAL PRACTICE

- Do not perform universal thyroid screening in pregnancy
- Ensure woman has adequate iodine intake in pregnancy (250 micrograms(ug)/day) from diet and supplementation. Most supplements contain 150ug iodine
- Take a detailed history with regards to current or past thyroid disease
- Refer woman with current or past history of hyperthyroidism (even if they are now euthyroid/hypothyroid post treatment) to Obstetric Medical Clinic or private endocrinologist familiar with thyroid disease in pregnancy, with the following test results:
    - Thyroid Function Tests (TFTs) – Thyroid Stimulating Hormone (TSH), free thyroxine (fT4), free triiodothyronine (fT3)
    - Thyroid Receptor Antibody (TRAb)
    - Thyroid Peroxidase Antibody (TPOAb)
- Review any recent Thyroid Function Test (TFTs) results - follow Appendix 1 for management
- Perform TSH for woman with history or symptoms of thyroid disease, ideally after 9 weeks' gestation, including woman already on thyroid treatment.
- Use trimester specific ranges for each pathology laboratory. If laboratory does not have trimester specific ranges, then use the following (as per RANZCOG policy statement):

TRIMESTER	TSH level (mIU/L)
First	0.1-2.5
Second	0.2-3.0
Third	0.3-3.0

- Refer to Appendix 1 for management of abnormal TFTs in pregnancy at RHW
- Refer to Obstetric Medical Clinic or private endocrinologist familiar with thyroid disease in pregnancy, as per Appendix 1 if TFTs are abnormal in pregnancy
- Follow documented management plan from Obstetric Medical Clinic/Private endocrinologist

Management during pregnancy

Overt or subclinical hypothyroidism (SCH)

- Assess woman clinically for symptoms or signs of hypothyroidism. There may be significant overlap with symptoms of normal pregnancy, especially in the first 16 weeks
- Recheck TSH, fT4 and fT3 at 6-8 weekly intervals during pregnancy
- Increase thyroxine treatment as required, guided by trimester specific normal ranges, with an emphasis on TSH as this is the most reliable TFT in pregnancy
- Recheck TFTs after commencement or adjustment of thyroxine treatment

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THYROID DISEASE IN PREGNANCY cont'd

Overt or subclinical hyperthyroidism

- Refer for assessment and management to the Obstetric Medical Clinic or a private endocrinologist familiar with thyroid disease in pregnancy
- Measure TRAb in early pregnancy and again in the third trimester in woman with thyrotoxicosis or a history of Graves' disease because of the rare risk of fetal or neonatal thyrotoxicosis
- Refer TRAb positive woman to Maternal Fetal Medicine (MFM) for assessment and management plan
- Treat with antithyroid drugs if required. Propylthiouracil (PTU) is the preferred agent in the first trimester although Neomercazole or Carbimazole may be substituted after 10-12 weeks' gestation. Titrate to maintain the fT4 and fT3 in the trimester specific normal range.
- Monitor TFTs 4-8 weekly depending on the clinical status

Management Postpartum

Management of treated subclinical or overt hypothyroidism in the immediate postpartum period

- **On thyroxine prior to pregnancy**
  - Reduce thyroxine dose back to non-pregnant dose immediately after delivery, and recheck TFTs after 4-6 weeks

- **SCH or woman who was not on thyroxine prior to pregnancy**
  - Reduce dose of thyroxine by 50% if pregnancy thyroxine dose ≥ 100 ug/day
  - Cease thyroxine if pregnancy dose <100 ug/day
  - Recheck TFTs in 4-6 weeks
  - Attempt to withdraw thyroxine, especially in woman who is TPOAb negative

TPOAb positive

- Observe TPOAb positive women clinically as she is at significant risk (60-70%) of manifesting either transient hyperthyroidism followed by hypothyroidism, or worsening hypothyroidism
- Check TFTs at 4 and 12 weeks' postpartum, or if symptoms develop

Subclinical or overt hyperthyroidism in the immediate postpartum period

- Continue antithyroid drugs
- Check TFTs at 4 weeks' postpartum

6. DOCUMENTATION

- ObstetriX
- Integrated Clinical Notes
- eMEDS
- Antenatal Card

7. EDUCATIONAL NOTES

- Comprehensive guidelines exist for management of thyroid disease in pregnancy.
- Pregnant women are recommended to ingest iodine 250ug/day. In 2007, a study demonstrated that Australian women are currently mildly iodine deficient, with a mean intake of 100ug/day. Therefore, the recommendation for women trying to conceive or pregnant, is to take 150ug of iodine each day as a supplement. Most supplements contain 150ug iodine.

THYROID DISEASE IN PREGNANCY cont'd

- Universal screening for thyroid dysfunction is not recommended however risk factors for screening (recommended by American Thyroid Association) are:
    - Symptoms of thyroid disease
    - Personal or family history of thyroid disease
    - Personal history of positive TPOAbs
    - Type 1 diabetes mellitus or other autoimmune disease
    - Personal history of head and neck radiation
    - Personal history or recurrent miscarriage and/or reduced fertility
    - BMI >35
- TSH falls in the first trimester, increasing towards non-pregnant levels in the second and third trimesters.
- Measuring TSH prior to 9-11 weeks will tend to overestimate the incidence of SCH. Recognise that the pregnancy related fall in TSH does not reach a nadir until 9-11 weeks' gestation.
- Overt hypothyroidism is defined as a raised TSH and reduced fT4 and fT3 as per trimester specific normal ranges, prior to thyroxine therapy. This is associated with adverse pregnancy outcomes and should be treated. Thyroxine treatment should be commenced immediately in this condition.
- SCH is defined as elevated TSH and normal fT4 and fT3 as per trimester specific ranges. This affects up to 2.5% of pregnant women. Of these 85% will be thyroid antibody positive. SCH should be considered an indicator of potential hypothyroidism. The impact on pregnancy outcomes is uncertain and therefore treatment of this group is controversial. Treatment with thyroxine may reduce miscarriage and preterm birth. A well conducted randomised control trial (RCT) of thyroxine treatment with SCH demonstrated no difference in neurological outcome.
- Thyroid antibody positivity i.e. thyroid peroxidase(TPO) or thyroglobulin(TG) antibodies is an asymptomatic condition which is associated with an increased risk of thyroid dysfunction in the future. These women may be at increased risk of subfertility and miscarriage. However, treatment with thyroxine has not been shown to reduce the risk of miscarriage. Similarly, in women undergoing fertility treatment, thyroxine does not improve pregnancy rates.
- In women with hyperemesis gravidarum who also have suppressed TSH levels, treatment of hyperthyroidism should not be undertaken without evidence of intrinsic thyroid disease (including goitre and/or thyroid autoantibodies). These women should be referred to the Obstetric Medical Clinic or a private endocrinologist familiar with thyroid disease in pregnancy.
- Subclinical hyperthyroidism is defined as a suppressed TSH but normal fT4 and tT3 as per trimester specific normal ranges.
- Overt hyperthyroidism is defined as a suppressed TSH and elevated fT4 and fT3 as per trimester specific normal ranges. Uncontrolled maternal hyperthyroidism has been associated with fetal tachycardia, small for gestational age babies, prematurity, stillbirths and possibly congenital malformations. This is why it is important to treat hyperthyroidism in the mother.
- Graves' disease is an autoimmune disorder caused by the production of TRAbs that stimulate the thyroid gland. These antibodies do cross the placenta and can interact with the fetal thyroid. Although uncommon (2-5% of cases of Graves' disease in pregnancy), high or increasing levels of maternal TRAbs have been known to cause fetal or neonatal hyperthyroidism.
- It is difficult to find what constitutes 'high' levels of TRAbs, but, general expert consensus opinion considers 'high' as $\geq$2-3 x upper limit of laboratory specific normal

THYROID DISEASE IN PREGNANCY cont'd

- In the woman with Graves' disease requiring antithyroid drug therapy, fetal hyperthyroidism due to the woman's TRAbs is rare, since the antithyroid drugs also cross the placenta. Of potentially more concern to the fetus/neonate is the woman with prior treatment for Graves' disease (for example radioactive iodine or surgery) who no longer requires antithyroid drugs.
- Postpartum thyroiditis most commonly presents with isolated hypothyroidism, but a biphasic presentation, and isolated hyperthyroidism can occur: a high index of suspicion is warranted for diagnosis.

8. RELATED POLICIES PROCEDURES CLINICAL PRACTICE LOP

- Hyperemesis Gravidarum and Nausea and Vomiting in Pregnancy – Management
- ACM Guidelines Consultation and Referral

9. RISK RATING

- High

10. NATIONAL STANDARD

- CC - Comprehensive Care

11. REFERENCES

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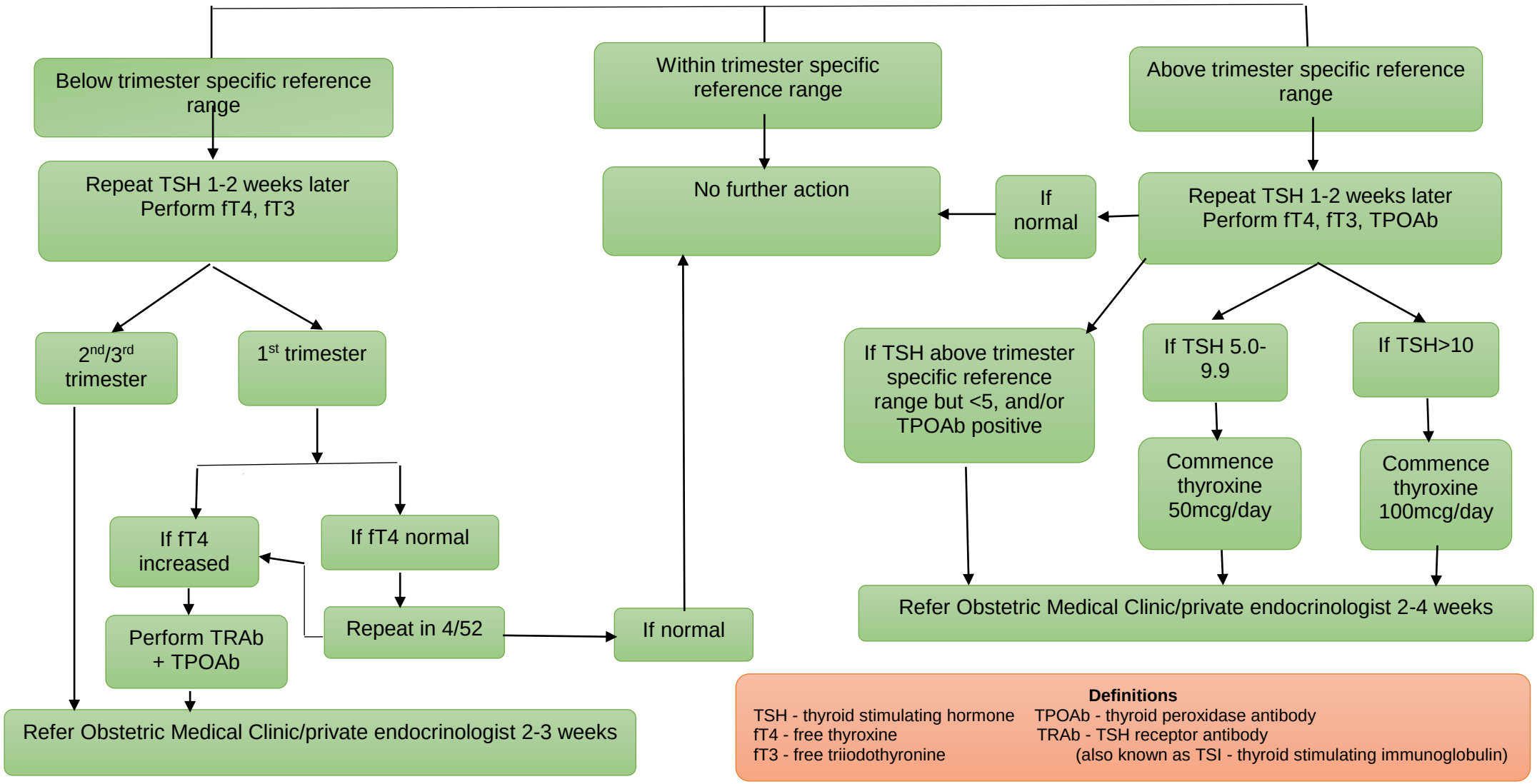
REVISION & APPROVAL HISTORY

Reviewed and endorsed Maternity Services LOPs group 25/10/16
Approved Quality & Patient Safety Committee 21/11/13
Endorsed Obstetrics LOPs 5/11/13

FOR REVIEW : NOVEMBER 2018

APPENDIX 1


TSH (ideally after 9 weeks' gestation)
mIU/l
Below trimester specific reference range
Within trimester specific reference range
Above trimester specific reference range
Repeat TSH 1-2 weeks later
Perform fT4, fT3
No further action
If normal
Repeat TSH 1-2 weeks later
Perform fT4, fT3, TPOAb
2nd/3rd trimester
1st trimester
If TSH above trimester specific reference range but <5, and/or TPOAb positive
If TSH 5.0-9.9
If TSH>10
If fT4 increased
If fT4 normal
Commence thyroxine 50mcg/day
Commence thyroxine 100mcg/day
Perform TRAb + TPOAb
Repeat in 4/52
If normal
Refer Obstetric Medical Clinic/private endocrinologist 2-4 weeks
Refer Obstetric Medical Clinic/private endocrinologist 2-3 weeks
Definitions
TSH - thyroid stimulating hormone
fT4 - free thyroxine
fT3 - free triiodothyronine
TPOAb - thyroid peroxidase antibody
TRAb - TSH receptor antibody
(also known as TSI - thyroid stimulating immunoglobulin)