



Diagnostic Investigations for Midwives: Thyroid, Hypertension, and Cholestasis

Thu Feb 3, 2022 | 1200-1300

Speaker: Dr. Brenda Wagner, Obstetrician

Q&A: Slido.com #midwives




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LAND ACKNOWLEDGMENT

I acknowledge that I am on the traditional Lands of the Xwsepsum (Esquimalt) and Lekwungen (Songhees) ancestors and families.

I would also like to recognize that some of you are joining us today from other regions of the province and acknowledge the traditional owners and caretakers of those lands.



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DISCLOSURE

I have no conflicts of interest to disclose.



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Learning Objectives

- When to order TSH and Free T4
- What other thyroid tests are important?
- When to order investigations for Cholestasis
- When should I do investigations for hypertension in pregnancy and what does it mean?
- Interpret investigations to assist with ongoing care

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Thyroid Disorders in Pregnancy

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When to do a TSH in pregnancy- What do you think?


1. Routinely in first trimester.
2. With hypothyroidism and on treatment
3. Experiencing excessive fatigue, feeling cold and constipation should have a TSH.
4. With IDDM or autoimmune disease (e.g. celiac) should have a TSH checked in pregnancy.
5. With hyperemesis.
6. With tachycardia, increased sweating, and diarrhea.

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When Thyroid Tests Make a Difference

| | |
|---------------------------------------|-------------------------------|
| Signs and symptoms of hyperthyroidism | Hyperemesis |
| Signs and symptoms of hypothyroidism | IDDM and autoimmune disorders |



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Signs and Symptoms of Hyperthyroidism

| | | | |
|---------------------------------------|--------------------------|---------------------------|-------------------------------|
| Weight loss | Tachycardia | Arrythmia or palpitations | Increased appetite |
| Nervousness, anxiety and irritability | Tremor | Sweating & Overheating | More frequent bowel movements |
| Enlarged Thyroid | Fatigue, muscle weakness | Difficulty sleeping | Skin thinning |

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Why is it important to diagnose and treat hyperthyroidism?


- Inadequately treated maternal hyperthyroidism can result in preterm labour and pre-eclampsia.
- Women with active Graves' disease during pregnancy are at higher risk of developing severe hyperthyroidism and thyroid storm.
- Graves' disease often improves during the third trimester of pregnancy and may worsen during the post partum period.

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When Thyroid Tests Make a Difference

| | |
|---------------------------------------|-------------------------------|
| Signs and symptoms of hyperthyroidism | Hyperemesis |
| Signs and symptoms of hypothyroidism | IDDM and autoimmune disorders |



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Transient Hyperthyroidism and Hyperemesis Gravidarum

- Transient Hyperthyroidism occurs in about 60% of patient with hyperemesis gravidarum
- Patients with transient hyperthyroidism have no previous thyroid illness, goitre is usually absent, and thyroid antibodies are negative
- A small proportion of these patients have clinical thyrotoxicosis

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When Thyroid Tests Make a Difference



| | |
|--|-------------------------------|
| Signs and symptoms of hyperthyroidism. | Hyperemesis. |
| Signs and symptoms of hypothyroidism. | IDDM and autoimmune disorders |

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Signs and Symptoms of Hypothyroidism

| | | | |
|-----------------|-----------------------------------|--|------------------------|
| Feeling tired | Unable to stand cold temperatures | Hoarse voice | Swelling of the face |
| Weight gain | Constipation | Skin and hair changes, including dry skin and loss of eyebrows | Carpal tunnel syndrome |
| Slow heart rate | Muscle cramps | Trouble concentrating | |


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Pregnancy Complications and Hypothyroidism

- Risk of miscarriage
- Association with anemia
- Muscle pain, weakness
- Pre-eclampsia
- Placental abnormalities
- Postpartum hemorrhage (bleeding)

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When Thyroid Tests Make a Difference



| | |
|--|-------------------------------|
| Signs and symptoms of hyperthyroidism. | Hyperemesis. |
| Signs and symptoms of hypothyroidism. | IDDM and autoimmune disorders |

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Other Conditions Associated With Hypothyroidism

- Celiac Disease
- Sjogren's Syndrome
- Pernicious Anemia
- Type 1 or Type 2 Diabetes
- Rheumatoid Arthritis
- Lupus

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Guidelines for Management of Thyroxine from Calgary, Alberta

For pregnant people already on levothyroxine

- Increase levothyroxine by two additional tablets per week once pregnancy is confirmed avoids development of overt hypothyroidism among most women.
 - Example: A woman on levothyroxine 100 mcg/day with TSH 3.5 mIU/L prior to conception should take levothyroxine 100mcg/day Monday to Friday and 200mcg/day on Saturday and Sunday or levothyroxine 125 mcg/day once pregnant.
- To avoid iatrogenic hyperthyroidism, if preconception thyroid stimulating hormone (TSH) is known to be <1.2 mIU/L, maintain preconception levothyroxine dose.
- Monitor TSH at time of pregnancy confirmation and every 4 weeks less than 20 weeks gestation or until stable TSH is achieved within gestational age specific reference ranges (see table below) then q trimester thereafter.
- Adjust levothyroxine to achieve and maintain TSH within gestational age specific reference ranges.
- Postpartum women should return to their pre-pregnancy levothyroxine dosage and have a TSH checked 6 weeks postpartum to ensure it is normal. Counsel patients to avoid co-ingestion of levothyroxine with iron or calcium supplements.*

*<https://www.departmentofmedicine.com/Endocrinology/endo-clinics/endo-endocrine-pathways/endo-thyroid-function-pregnancy/>

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There is no evidence of benefit to universal TSH screening

When do Thyroid Tests Make a Difference

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What does that TSH or T4 mean?

| Weeks Gestation | TSH mIU/L | Free T4 pmol/L | Free T3 pmol/L | Total T4 nmol/L |
|-----------------|-----------|----------------|----------------|-----------------|
| 4 to 8 | 0.1 - 4.0 | 10 - 25 | 3.5-6.5 | Not applicable |
| 9 to 12 | 0.1 - 3.0 | 11 - 22 | 3.5 - 6.0 | Not applicable |
| 13 to 27 | 0.1- 4.0 | 10 - 19 | 3.5-6.0 | 90 - 180 |
| 28 to term | 0.5 - 5.0 | 9.0-17 | 3.0-5.2 | 75 - 190 |

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Someone checked a TSH

?Hypothyroid

TSH>10mIU/L

- Start levothyroxine
- Monitor TSH every 4 weeks if < 20 weeks gestation or until TSH steady
- Then TSH q trimester to ensure that it remains normal.
- Postpartum: 20% dosage reduction of levothyroxine and check TSH 6 weeks postpartum

TSH ≥ 5mIU/L and <10mIU/L

- Repeat in 2 weeks:
- If TSH if persistently > 5 mIU/L and <10mIU/L - No evidence of benefit of Levothyroxine
- If decision to start levothyroxine is made use low dose (i.e. 50 mcg/day.)
- If levothyroxine initiated stop postpartum and recheck TSH at 6 to 12 weeks

if TSH ≤ 5 mIU/L – no further intervention or labs tests required

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Someone checked a TSH

?Hyperthyroid

If TSH 0.1 to <5 mIU/L

- No further intervention or lab testing of TSH or antithyroid peroxidase antibodies required (1, 3, 4)

If TSH <0.1 mIU/L

- Check Free T4 and Free T3
- If Free T4 or Free T3 elevated above gestational age specific reference ranges (in table below), Endocrinology or Internal Medicine referral


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Good Websites for Patients

<https://www.nidk.nih.gov/health-information/endocrine-diseases/hypothyroidism>

<https://www.thyroid.org/>

<https://www.hopkinsmedicine.org/health/conditions-and-diseases/staying-healthy-during-pregnancy/hypothyroidism-and-pregnancy>



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When to do a TSH - What do you think?

1. All pregnant people should have a TSH in pregnancy
NO
2. Pregnant people with a history of hypothyroidism and on treatment should have a TSH checked
YES
3. Pregnant people reporting excessive fatigue, feeling cold and constipation should have a TSH
YES
4. Pregnant people with IDDM or autoimmune disease (e.g. celiac) should have a TSH checked in pregnancy
YES
5. Pregnant people with hyperemesis should have a TSH checked
YES
6. Pregnant people with tachycardia, increased sweating, and diarrhea should have a TSH checked.
YES

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A word about Thyroid Antibodies

- Thyroid autoimmunity refers to the presence of antibodies to thyroperoxidase or thyroglobulin or thyroid-stimulating hormone receptor antibodies
- Present in 18% of pregnant patients
- Post-partum thyroiditis is substantially more frequent in those who have thyroid antibodies during pregnancy than in those who do not
- Neonatal complications are not as common as previously thought. Measurement of antibodies is mostly for maternal complications.

Balucan FS, Morshed SA, Davies TF. Thyroid autoantibodies in pregnancy: their role, regulation and clinical relevance. *J Thyroid Res.* 2013;2013:182472. doi:10.1155/2013/182472

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Intrahepatic Cholestasis of Pregnancy (ICP)

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Cholestasis

- Jo is G3 P2 at 19 wks with an uncomplicated pregnancy comes for a routine prenatal visit. They report the onset of itching.
- mostly on their abdomen.
- It is worse right after bathing.

Should you check bile salts?

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- Should you check bile salts?

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Pruritis in Pregnancy

- Pruritis affects 20% of pregnant people
- The most common cause of pruritis in pregnancy is dry skin
- Usually worse over the abdomen and can have an onset at any time in pregnancy
- Other causes of pruritis need to be considered

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Cholestasis

- Cia is a G1P0 at 32 weeks. Healthy, uncomplicated pregnancy. They have developed severe itching
- It started mostly on their hands and feet but now it is almost everywhere.
- It is worse at night
- They are finding it hard to sleep

Should you check bile salts?

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- Should you check bile salts?

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Cholestasis

- North America Average is 0.5-1%
- More common in winter in Scandinavia and Chile higher (15-28%)
- occurs after 20 weeks gestation
- Pruritis may start on hands and feet and may become so severe it is interfering with sleep
- It does not usually improve with moisturizers or antipruritic remedies
- Usually has no visible skin changes unless excoriations are present.

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Complications of Cholestasis

ICP is associated with several adverse perinatal outcomes

- Stillbirth
- meconium-stained amniotic fluid
- preterm birth -spontaneous and iatrogenic.

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Bile Salts – When to Check and What they mean

- Little difference between fasting & random bile acids
- If pruritis persists, repeat bile acids - but weekly testing not recommended
- Bile Salts > 10 considered diagnostic of ICP (limited data and accuracy unclear)
- To prevent stillbirth recommend early intervention (36+0) if bile salts $\geq 100 \mu\text{mol}$
- Cochrane – “The diagnostic accuracy of total serum bile acids for intrahepatic cholestasis of pregnancy might have been overstated”

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Management Based on Bile Acid Level – SMFM 2020

| Bile Acid Level | Antenatal Surveillance | Induction | Repeat Bile Acids |
|--------------------|--|---|--|
| ≥ 100 µmol/L | Yes, start when patient would be delivered if abnormal | Offer delivery at 36+0 | No need to repeat Follow transaminases |
| ≥ 40 - <100 µmol/L | Yes, start when patient would be delivered if abnormal | Offer delivery 37+0 to 39 Timing depends on severity of symptoms and bile acid level | Repeat close to 36 weeks to inform timing of delivery. If rising, consider repeat and transaminases. |
| ≥ 10 < 40 µmol/L | Yes, start when patient would be delivered if abnormal | Offer delivery 37+0 to 39 Timing depends on severity of symptoms and bile acid level | Repeat close to 36 weeks to inform on timing of delivery. If rising, consider repeat and follow transaminases. |
| < 10 µmol/L | No | Usually after 39 weeks. Base on maternal symptoms | If symptoms persist consider repeat at 36 weeks. |

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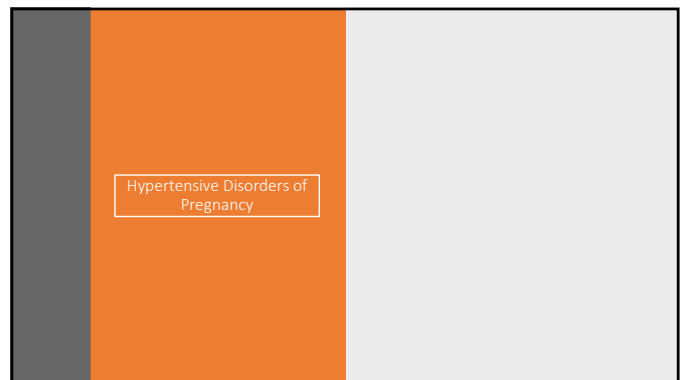


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Hypertensive Disorders of Pregnancy

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Hypertensive Disorders of Pregnancy (HDP)

- When to do tests
- What tests to do
- How to Interpret

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Definitions for HDP

- Gestational Hypertension (onset after 20 weeks)**
 - OFFICE/Hospital - SBP ≥140 mmHg or DBP ≥ 90 mmHg - same arm at least 15 minutes apart after 10 min rest
 - HOME: SBP ≥ 135 mm Hg or DBP ≥ 85 mm Hg.**
- Chronic Hypertension**
 - Prepregnancy OR
 - Onset prior to 20 weeks gestation
- Severe -**
 - SBP ≥ 160 mmHg OR
 - DBP ≥ 110 mmHg
- Preeclampsia -** Chronic or GHTN with one or more of the following new onset conditions:
 - Proteinuria
 - Other maternal organ dysfunction (renal, hepatic, neurological, hematologic)
 - Uteroplacental dysfunction (fetal growth restriction)

** See Canadian Hypertensive Guidelines 2020

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Risks of hypertension

- Hypertension is 2nd most common cause of direct maternal mortality in Canada. (PHAC, 2017)
- Pre-eclampsia risk increases with hypertension:
 - 21 % with CH
 - 25% with GH
 - 35% with GH Dx < 34 weeks
 - 12% with white coat HTN

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Should you do Lab Tests?

- A healthy G1 with BP 135/85 mmHg in the office on one occasion
- A healthy G1 with white coat hypertension and BP 135/85 at home on 2 occasions*
- A patient with IDDM and elevated creatinine in early pregnancy
- Anyone in pregnancy with a history of hypertension

See Canadian Hypertensive Guidelines 2020

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When to Do Lab Tests

- Diagnostic Criteria for Gestational Hypertension have been met
- High risk of Gestational Hypertension based on screening
 - e.g. EMMA clinic with moderate or high risk of HDP
- In Pregnancy with Chronic Hypertension, particularly pre-pregnancy Type 1 or Type 2 diabetes or renal disease.
- Rising bp and proteinuria or normal blood pressure and signs or symptoms of preeclampsia – do a Urine PCR and if abnormal do bloodwork.

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Laboratory Investigations

- CBC
- Creatinine, Na, K, Uric Acid
- Liver enzymes – AST* or ALT, LDH
- Urine protein
 - Urine PCR > 30 mg/mmol
 - Only repeat when ≤ 30 mg/mmol
- Others as clinically indicated
 - PTT, INR, Fibrinogen – only when plts abnormal
 - Glucose, bilirubin,
 - Albumin
 - GBS

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Lab Normal Values in Pregnancy

| Test | Normal Value | Pregnancy | Test | Normal Value | Pregnancy |
|----------------|----------------|---------------|-----------|-----------------|----------------|
| Albumin | 35-50 g/L | 25-40 g/L | AST | 7-40 IU/L | 7-40 IU/L |
| Creatinine (s) | 50-110 µmol/L | 30-80 µmol/L | ALT | 5-35 IU/L | 5-35 IU/L |
| Hemoglobin | 120-160 g/L | 100-144 | Platelets | 150-400 x 109/L | SI. Decrease |
| Hematocrit | 0.37-0.47% | 30-40% | Sodium | 135-145 mmol/L | 131-143 mmol/L |
| Uric Acid | 120-420 µmol/L | 90-300 µmol/L | Potassium | 3.5-5.1 mmol/L | 3.2-4.9 mmol/L |
| LDH | 45-90 IU/L | 45-90 IU/L | | | |

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Lab Values in Preeclampsia

| Test | Pregnancy | Preeclampsia | Test | Pregnancy | Preeclampsia |
|----------------|---------------|--------------|-----------|----------------|--------------|
| Albumin | 25-40 g/L | Decreased | AST | 7-40 IU/L | Increased |
| Creatinine (s) | 30-80 µmol/L | Increased | ALT | 5-35 IU/L | Increased |
| Hemoglobin | 100-144 | Decreased | Platelets | SI. Decrease | Decreased |
| Hematocrit | 30-40% | Increased | Sodium | 131-143 mmol/L | ?Decreased |
| Uric Acid | 90-300 µmol/L | Increased | Potassium | 3.2-4.9 mmol/L | ?Decreased |
| LDH | 45-90 IU/L | Increased | | | |

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Should you do Lab Tests?

- A healthy G1 with BP 135/85 mmHg in the office on one occasion - **NO**
- A healthy G1 with white coat hypertension and BP 135/85 at home on 2 occasions - **YES**
- A patient with IDDM and elevated creatinine in early pregnancy - **YES**
- A patient who presents for prenatal care with a history of hypertension - **YES**

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Evaluation of Fetus

- Fetal Movement Count**
 - Daily
- NST**
 - Stable Preexisting Hypertension
 - At 35 weeks – weekly
 - GHTN or Preeclampsia
 - At diagnosis - 2x/week
- Ultrasound**
 - Fetal size & growth - biweekly
 - Amniotic fluid – 2x/week
 - Umbilical artery Doppler – 2x/week

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PIERS Calculator

<https://pre-empt.obgyn.ubc.ca/home-page/past-projects/fullpiers/>
 Chest Pain
 SpO₂
 Platelets
 Creatinine
 AST/ALT

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Antenatal risk assessment for placentally mediated pregnancy complications

Evaluating Maternal and fetal Markers of Adverse placental outcomes (EMMA)

- ≥1 Major risk factor:**
 - Chronic renal disease
 - Anti Phospholipid Antibody Syndrome
 - Chronic hypertension
 - Diabetes with evidence of end organ disease
 - Chronic/Active Autoimmune disease
 - Maternal age ≥40 + nulliparity
 - Previous (I) severe pre-eclampsia
 - Or (II) IUGR resulting in delivery <34 weeks
 - Previous unexplained stillbirth
 - First or second trimester heavy menstrual-like bleeding
 - Fetal 2nd trimester echogenic bowel
 - Other...
- ≥2 abnormal analytes**
 - PAPP-A ≤ 0.15 MoM
 - uE3 ≤ 0.40 MoM
 - AFP ≥ 2.5 MoM
 - hCG ≥ 4.0 MoM
 - Inhibin A ≥ 3.0 MoM
- And/Or**
 - 1 severely abnormal analyte**
 - AFP ≥ 3.5 MoM
 - hCG ≥ 4.5 MoM
 - Inhibin A ≥ 4.0 MoM
- ≥3 minor risk factors:**
 - Nulliparity
 - Maximal age <20 or >35
 - BMI <20 or >35
 - IVF pregnancy
 - Pre-existing diabetes
 - Pregnancy interval <6 or >60 months
 - Any previous pre-eclampsia or IUGR
 - Smoking ≥5 cigarettes per day
 - Single abnormal maternal serum analyte
 - PAPP-A ≤ 0.15 MoM
 - uE3 ≤ 0.40 MoM
 - AFP ≥ 2.5 MoM
 - hCG ≥ 4.0 MoM
 - Inhibin A ≥ 3.0 MoM

Start ASA 81 mg daily ≤ 16 weeks GA
 Start Calcium 1g/d if daily intake is <600mg/d
 book detail ultrasound at 19-20 weeks
 Eligible for BCW EMMA Clinic consultation (attach risk assessment form to MFM referral)

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References and Resources

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- <http://www.bcwomens.ca/Pregnancy-Prenatal-Care-Site/Documents/BCW%20EMMA%20Clinic%20referral.pdf>
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