PERI-PREGNANCY DRUG TREATMENT CONSIDERATIONS
PRE-CONCEIVED NOTIONS

April 2012

GUIDELINES

- **Diabetes – CDA $_{2008}$:** http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf
- **Hypertension–SOCG$_{2008}$:** http://www.sogc.org/guidelines/documents/gui206CPG0803hypertensioncorrection.pdf
- **Thyroid – ATA $_{2011}$:** http://thyroidguidelines.net/sites/thyroidguidelines.net/files/file/thy.2011.0087.pdf

OTHER RESOURCES

Briggs et al. ***Drugs in Pregnancy & Lactation.*** 9th ed. 2011.

USEFUL LINKS

- **FDA Pregnancy Exposure Registries:** http://www.fda.gov/ForConsumers/byAudience/ForWomen/default.htm
- **LactMed:** http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT

SASKATCHEWAN LINKS

- **Maternal Mental Health:** https://sites.google.com/site/maternalmentalhealthsk/
- **Saskatchewan Drug Information Service:** http://druginfo.usask.ca/
- **Saskatchewan Prevention Institute - HIV:** http://www.preventioninstitute.sk.ca/sexual-and-reproductive-health/hivaids-and-reproductive-health

RXFILES RELATED Q&A

Antidepressants During Pregnancy & Breastfeeding
http://www.rxfiles.ca/rxfiles/uploads/documents/Antidepressants-PregnancyandBreastfeeding-QandA.pdf

Diabetes in Pregnancy & GDM
http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Pregnancy-QandA.pdf

Vitamin D
http://www.rxfiles.ca/rxfiles/uploads/documents/Vitamin-D-Overview-QandA.pdf

RXFILES RELATED CHARTS 8th ed

Pre-Conception Patient Case

A 34 year old female with a history of T2DM, proteinuria & hypothyroidism, has a routine visit to refill her prescriptions. During your discussion with her, you find out she recently married. She & her husband would like to have a family, but have not yet started trying to conceive. She is currently on metformin 850mg po bid, losartan 100mg po daily & levothyroxine (LT4) 125mcg po daily. She does not take any herbals, vitamins or minerals. Her BP is currently 132/90mmHg, BMI 36kg/m^2, and most recent A1C was 8.2%, ACR 3.2mg/mmol, CrCl 118ml/min, and TSH 3.4mIU/L. She has had no prior pregnancies, does not exercise & has poor nutrition.

How do you address her pre-conception needs?

- Due to the high rate of unplanned pregnancies, consider pre-conception counseling during every patient visit with females of childbearing potential, especially when comorbid conditions exist.
- **Her BMI > 35kg/m^2 & diabetes put her at high risk of fetal neural tube defects**. Start folic acid 5mg po daily, ideally for 3 months prior to conception & continue throughout the 1st trimester. Reduce dose to 0.4-1mg po daily for 2nd & 3rd trimesters, & for 6 weeks postpartum or while breastfeeding.
- **Continue metformin and add insulin**. Target a pre-conception A1C <7% (<6% if can be done safely and without hypoglycemia). Educate the patient regarding more frequent BG monitoring.
- **Continue her losartan until pregnancy confirmed** & then switch her to a safer alternative (see Hypertension: Peri-Pregnancy in next column).
- **Increase her LT4 dose & target a pre-conception TSH <2.5mIU/L.** Once pregnancy confirmed, she may increase her dose by 2 pills per week (i.e. ↑ from 7 to 9 pills/week).

Other considerations:

- Encourage activity (e.g. walking) & healthy nutrition.
- Assess & advise on smoking, alcohol & caffeine.
- Supplement with vitamin D 600 IU – 2000 IU/day.
- Promote adequate calcium 1000mg/day (diet ± supplement).

Quiz: (see inside chart for answers)

- When should pre-conception counseling start?
- Which patients should receive folic acid 5mg/day?
- Which blood glucose management medications can be used during pregnancy?
- What is the pre-conception target for TSH in hypothyroid patients?
- Should ACEI/ARBs always be discontinued prior to conception?

Diabetes: Peri-Pregnancy Management

- Elevated A1C prior to, & during pregnancy can cause maternal & fetal/infant morbidity & mortality.
- Start folic acid 5mg po daily prior to conception.
- Insulin: most safety data e.g. NPH, lispro, aspart, regular.
- Metformin & glyburide may be continued in T2DM, or used in Gestational DM if non-adherent to or refuse insulin. Not thought be to be teratogenic, & similar to insulin in maternal & fetal outcomes. Add insulin to metformin if needed to achieve targets.
- Pregnancy Glycemic Targets:
  - FBG 3.8-5.2, 1-hr BG 5.5-7.7, 2-hr BG 5-6.6
- Females with GDM are at high risk of T2DM. Screen for T2DM between 6 weeks & 6 months postpartum. Consider annual screening thereafter.

Hypertension: Peri-Pregnancy Management

- Reassess the need for antihypertensive therapy before & during pregnancy as blood pressure tends to drop until 16-20 weeks gestation.
- Discontinue statins & atenolol prior to conception.
- Historically, ACEI/ARBs were contraindicated during pregnancy but recent evidence suggests these medications are safe during 1st trimester. It is reasonable to wait until pregnancy is confirmed before switching an ACEI/ARB to another agent, especially when used for nephropathy. If used for HTN, may switch prior to conception. **ACEI/ARBs are still contraindicated during 2nd & 3rd trimester.**
- Labetalol, methyldopa & nifedipine XL continue to be 1st line agents for the treatment of HTN disorders during pregnancy.
- Diastolic BP should not be ↓ too rapidly & ideally be ≥80mmHg to maintain placental perfusion.
- Low-dose ASA may be used for ↓ cardiovascular risk &/or preeclampsia in at risk patients see chart (pg 2).
- Continue antihypertensive postpartum to cover BP peak seen 3-5 days after delivery, then reassess.

Hypothyroid: Peri-Pregnancy Management

- TSH Pregnancy Goals: 1st trimester ≤2.5mIU/L, 2nd & 3rd trimester ≤3.5mIU/L.
- Aim for a pre-conception TSH of <2.5mIU/L.
- ↑ LT4 dose by 2 extra pills/week once pregnancy confirmed (i.e. ↑ from 7 to 9 pills/week). Check TSH in 4 weeks.
  - May instruct patient to increase the dose independently upon missed menstrual cycle or after a positive home pregnancy test, & to notify physician as soon as possible.
- Post-partum: return the patient to her pre-pregnancy LT4 dose. May need to adjust the dose depending on the amount of weight gained.

Motherisk: Treating the mother, protecting the unborn

- Excellent resource for both healthcare professionals & patients. Website: http://www.motherisk.org
- **Hotlines:** 1-877-327-4636 Alcohol & Substance; 1-877-439-2744 Motherisk Helpline; 1-800-436-8477 Morning Sickness; 1-888-246-5840 HIV & HIV Treatment

Peri-Pregnancy Drug Treatment Considerations ♀

prepared by: Lynette Kosar BSP, MSc www.RxFiles.ca April 2012

~ ½ OF PREGNANCIES (⅔ OF DIABETIC PREGNANCIES) ARE UNPLANNED. TREAT EVERY PATIENT VISIT WITH FEMALES OF CHILDBEARING POTENTIAL AS AN OPPORTUNITY FOR PRECONCEPTION COUNSELING.

See On-line Extras for Pregnancy & Lactation Lifestyle information (e.g. activity, nutrition, body weight, smoking, alcohol & caffeine)

	PRE-PREGNANCY (~3 MONTHS PRIOR) &/OR POTENTIAL FOR PREGNANCY	PREGNANCY Pregnancy P Safe, P Likely Safe, P Caution, P CI, P Unknown	POST-PARTUM & LACTATION Lactation L Safe, L Likely Safe, L Caution, L CI, L Unknown
Nutrition [1,2,3,4] see chart pg 97	PL **Ca^{++}** Total (diet ± supplement) 1.3g/day ≤18 yr, 1g/day ≥19 yr; PL **Vitamin D** Total 600 IU/day^{IOM} – 2000 IU/day^{CPeds}, consider periodic 25(OH) level; ⇨ P **Folic acid: dose based on risk of neural tube defect** • Low risk: 0.4-1mg po daily, initiate 2-3 months prior • High risk*: 5mg po daily, initiate 3 months prior ***High risk**: DM, BMI >35kg/m^2, medications (anticonvulsants, methotrexate, sulfonamide, trimethoprim), family hx of neural tube defect, etc (see Extras).	⇨ P **Folic acid: dose based on risk of neural tube defect** • Low risk: 0.4-1mg po daily throughout pregnancy • High risk: 5mg po daily 1st trimester, then ↓ 0.4-1mg po daily ⇨ P **Iron**: supplement with 16-30mg elemental po daily (UL 45mg/day)	PL **Vitamin A** retinol > 10,000 IU or 3000mcg/day (teratogenic) ⇨ L Folic acid 0.4-1mg po daily, continue 6 weeks post-partum or as long as breastfeeding continues ⇨ **Vitamin D** for term infants in 1st year: 400-800 IU/day. Infant formulas provide 400 IU/L (1L=34oz). Supplement [e.g. BABY D DROPS] breastfed & formula fed infants at risk of deficiency.
	Maternal Multivitamins: MATERNA▼ [Fe^{++} 27mg, folic acid 1mg, Ca^{++} 250mg, Vit D 400IU], PREGVIT/PREGVIT FOLIC 5^{Rx} [Fe^{++} 35mg, folic acid 1.1/5mg, Ca^{++} 300mg, Vit D 250IU], PALAFER CF [Fe^{++} 100mg, folic acid 0.5mg]. Generic & store brands also		
Diabetes [5,6] see charts pg 24-29b	PL Insulin (NPH$_{most\ data}$, lispro, aspart, regular); PL glyburide; PL metformin, insulin glulisine, insulin detemir, insulin glargine $_{limited\ data/theoretical\ risks}$; PL or PL for all others ⇨ Targets: A1C≤7%; (≤6% if can be safely achieved) • A1C≤7% ↓ risk of spontaneous abortions, malformations, preeclampsia, & maternal retinopathy • A1C >10% ↑↑ miscarriages & congenital malformations NICE DM Pregnancy Guidelines: strongly advises to avoid pregnancy if A1C >10% ⇨ Start folic acid **5mg** po daily ⇨ Insulin: most safety data daily injections or continuous subcutaneous infusions ⇨ Metformin & glyburide may be continued in T2DM, or used in GDM if non-adherent to or refuse insulin. Not thought to be teratogenic, & similar to insulin in maternal & fetal outcomes. Add insulin to metformin if needed to achieve targets.[7] ⇨ Screen: retinopathy, HTN, CKD; hypothyroidism if T1DM	⇨ **Gestational Diabetes (GDM):** Screen at 24-28 weeks 50g glucose load, or 75g OGTT • If ↑ risk for T2DM: screen for GDM 1st trimester; reassess 2nd & 3rd (age ≥35 years, family hx, hx of GDM, BMI ≥30kg/m^2, high-risk population) • Trial lifestyle changes x2 weeks before starting drug therapy • Walking 3-4x/week for 25-40min can ↓ insulin requirements[8] ⇨ **Pre-existing & Gestational Diabetes Targets:** • Desire tight BG control while avoiding hypoglycemia • A1C: ≤6% if possible, otherwise ≤7-8%; risks ↑↑ if A1C >10% • SMBG: preprandial, postprandial & occasional nighttime - FBG: 3.8-5.2; 1hr BG: 5.5-7.7; 2hr BG: 5.0-6.6. Avoid ketosis. ⇨ Screen: retinopathy 1st trimester; ACR & GFR every trimester if CKD	⇨ Use pre-pregnancy blood glucose targets ⇨ Screen: • Retinopathy within the 1st year post-partum • T1DM at ↑ risk of thyroiditis: TSH & FT4 6 wks post-partum • GDM at ↑ risk of T2DM: 75g OGTT $_{not\ A1C}$ between 6 weeks & 6 months post-partum. Consider annual screening thereafter. Also see RxFiles Q&A Diabetes in Pregnancy & GDM: http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Pregnancy-QandA.pdf
Hypertension [9,10] see HTN & CV Risk Reduction charts pg 2-7,10-11,15	P 1st line: labetalol 100-400mg po BID-QID, methyldopa 250-500mg po BID-QID, nifedipineXL 20-60mg po OD-BID 2nd line:verapamil, metoprolol, propranolol P Thiazides–appear safe, but ? effectiveness during pregnancy. P Avoid atenolol low birth weight: taper & switch to safer alternative. ⇨ Pre-existing HTN: reassess indication for drug tx. In otherwise healthy, mild-moderate HTN: consider ↓ dose or d/c agent. ⇨ **ACEI, ARB**: Recent data suggests ACEI & ARB risk of fetal toxicity during 1st trimester is not greater than other antihypertensives. HTN itself may contribute to fetal toxicity, perhaps not drug therapy.[11] If used for nephropathy, may wait until pregnancy confirmed before switching to alternative. ⇨ P Taper atenolol & switch to a safer alternative (see above) ⇨ Other cardiovascular risk reduction medications: P Low-dose ASA $_{if\ indicated}$, clopidogrel; P Statins ⇨ Obtain baseline serum creatinine, K$^+$, LFTs, & urinalysis. SOGC Guidelines: http://www.sogc.org/guidelines/documents/gui206CPG0803_001.pdf	⇨ BP ↓ (nadir 16-20 wks), & ↑ to pre-pregnancy levels near term. ⇨ GestHTN=HTN occurring ≥20wks; Severe HTN: ≥160/110mmHg ⇨ Non-severe HTN: 140-159/90-109mmHg. BP Goals: • **with** comorbid DM, renal or cerebrovascular dx: 130-139/80-89mmHg • **without** comorbid conditions: 130-155/80-105mmHg • DBP ≥80mmHg to maintain placental perfusion ⇨ P Avoid ACEI, ARB & atenolol: taper & switch to safer alternative ⇨ **Preeclampsia:** see Extras for definition, potential risk with supplements, etc. • High risk patients hx of preeclampsia, HTN, CKD, autoimmune dx, DM, proteinuria: P **ASA** 81mg po HS start before 16 wks gestation until delivery • Low & at risk women with low **Ca^{++}** dietary intake <600mg/day: P **Ca^{++} 1000mg po daily (in divided doses, max 500mg/dose)** • P Fish oils (dietary or evening primrose), vitamins E & C do not ↓ risk	⇨ Continue antihypertensive(s) post-partum to cover BP peak seen 3-5 days after delivery, then reassess. ⇨ BP goal: as per non-pregnant ⇨ NSAIDs may adversely impact BP control ⇨ L Enalapril, captopril, nifedipine XL, diltiazem, verapamil, labetalol, metoprolol, spironolactone, & hydralazine ⇨ L Hydrochlorothiazide, chlorthalidone: at therapeutic doses for treating HTN, do not appear to ↓ milk volume, suppress lactation or cause infant electrolyte abnormalities. ⇨ Methyldopa is considered safe during lactation; but, consider discontinuing it within 2 days after delivery due to ↑ risk of depression (especially if history of, or at risk of depression).
Thyroid [12,13] see charts pg 34-35	**HYPOTHYROIDISM:** PL Levothyroxine (LT4) $_{preferred}$, Liothyronine (LT3). Take LT4 or LT3 in am before breakfast or HS, and Fe^{++} & Ca^{++} supplements (including maternal vitamins) with lunch or supper. **HYPERTHYROIDISM:** 1st Trimester P propylthiouracil (PTU), P methimazole (MMI) congenital malformations; 2nd & 3rd Trimester: P MMI, P PTU risk of hepatotoxicity (0.1-0.2%). Lactation: L MMI$_{≤30mg/d,\ preferred}$, PTU$_{<300mg/d}$ **Hypothyroidism:** ⇨ Aim for pre-conception TSH of 0.5-2.5mIU/L ⇨ Thyroid requirements ↑ ≥25% in pregnancy. May educate patient to independently ↑ her LT4 dose by 2 pills/week (i.e. ↑ from 7 to 9 pills/wk) upon a missed menstrual cycle or positive home pregnancy test, & notify her physician as soon as possible. ⇨ Subclinical: monitor for progression. Check TSH & FT4 q4wks the first ½ of pregnancy & at least once between 26-32 wks. **Hyperthyroidism:** ⇨ Overt: ideally, conception postponed until euthyroid ⇨ Subclinical: not linked to adverse pregnancy outcomes. Treatment not recommended. ⇨ MMI ≥10x more potent than PTU (100mg PTU ≈ 5-10mg MMI)	**Hypothyroidism:** ⇨ TSH Goal: 1st trimester ≤2.5mIU/L, 2nd & 3rd trimesters ≤3.5mIU/L ⇨ Check TSH levels once pregnancy confirmed, then q4wks during the first ½ of the pregnancy & at least once between 26-32 wks. **Hyperthyroidism:** ⇨ Gestational: symptomatic tx only (N&V, dehydration); anti-thyroid drugs not indicated as FT4 levels will normalize by 14-18 weeks. ⇨ Graves: 1st trimester – may worsen, 2nd & 3rd – may improve. ~25% can discontinue drug therapy during 3rd trimester. • FT4 & TSH levels: q4wks, then q4-6wks after normal range achieved. FT4 – target at or slightly above the upper limit of normal as both PTU & MMI cross the placenta may be able to ↓ dose • Beta-blocker (e.g. Propranolol 20-40mg po q6-8h) may be used to control sx. Taper dose as clinically indicated; can often d/c in 2-6 wks.	**Hypothyroidism:** ⇨ Return patient to pre-pregnancy dose of LT4. May need to consider amount of weight gained during pregnancy. ⇨ Check TSH at 4-6 weeks post-partum visit ⇨ Hashimoto's Thyroiditis: >50% of females may require a dose higher than their pre-pregnancy dose **Hyperthyroidism:** Graves often flares post-partum **Post-partum Thyroiditis:** 32% will have isolated thyroxicosis, 43% isolated hypothyroidism, & 25% both phases ⇨ Hyperthyroid phase – may occur 2-6 months post-partum. If symptomatic, use a beta-blocker (e.g. propranolol 10-20mg po QID, gradually taper to discontinue). ⇨ Hypothyroid phase – may occur 3-12 months post-partum. Treat with LT4 for 6-12 months, reassess/taper.

Motherisk www.motherisk.org. Hotlines: 1-877-439-2744 Motherisk Helpline, 1-877-327-4636 Alcohol & Substance, 1-800-436-8477 Morning Sickness, 1-888-246-5840 HIV & HIV Treatment

Infectious Diseases[14,15,16,17,18,19,20,21,22,23]

Antibiotics			1st Trimester	2nd Trimester	3rd Trimester	Lactation
CEPHALOSPORINS						
FLUOROQUINOLONES			? malformations	safer alternatives usually available		
MACROLIDE	Erythromycin non-estolate					
	Erythromycin estolate ILOSONE		risk of maternal hepatoxicity			
	Azithromycin		limited data; no teratogenicity in humans or animals			
	Clarithromycin		malformations in animals & humans, but no definitive link			
PENICILLINS ± clavulanate						
TETRACYCLINES			abnormal teeth & bone development, malformations, maternal hepatoxicity			Tetracycline
						Doxy-, Mino-cycline
OTHER	Clindamycin					
	Cotrimoxazole BACTRIM	Sulfamethoxazole			hemolytic anemia,neonate jaundice, kernicterus	Ok in healthy term infants without G6PD deficiency
		Trimethoprim	↓ folic acid			
	Metronidazole (oral)		1st trimester: accumulated data suggests likely safe			May hold BF 12-24hr post-tx
	Nitrofurantoin				neonate hemolytic anemia	Avoid in G6PD deficiency
	Vancomycin					
Legend			Safe	Likely Safe	Caution	Contraindicated

Pre-Pregnancy **HIV:** (see charts pg 58-59) Assess safety of medications. **Mother-to-child transmission (mtct) of HIV is preventable**; consider universal screening as identification & treatment can ↓ risk of transmission to <2%.

Immunizations: (see chart pg 50) Update as required. Obtain rubella & varicella antibodies if unsure of immunization history. Delay conception for 1-3 months after live vaccines (e.g. MMR, varicella).

Sexually transmitted infections (STI): (see chart pg 55) Screen and treat.

Pregnancy **Asymptomatic Bacterial Vaginosis**: Screen & treat at 12-16 weeks in high risk pregnancies (e.g. previous pre-term delivery or premature rupture of membranes). Re-test 1 month after treating. F→P Metronidazole, P clindamycin. Topical does not protect against pre-term delivery, but as effective as oral for eradicating infection.

Genital Herpes Simplex Virus: **1st Symptomatic Episode:** P acyclovir or valacyclovir. Consider cesarean section if episode occurs late in 3rd trimester. **Recurrent:** Cesarean section is recommended if there is a lesion or prodome at delivery. P acyclovir 200mg po QID or 400mg po TID, or P valacyclovir 500mg po BID starting at 36 weeks will ↓ recurrence rates at delivery (NNT=9) & need for cesarean section (NNT=10), but limited data to suggest ↓ mtct.

Group B Strep +ve: P penicillin IV once labour starts; if allergy: cefazolin IV unless anaphylactic pen allergy, clindamycin IV if sensitive Asymptomatic GBS bacteriuria <100,000 CFU/ml should not be tx to prevent maternal/perinatal adverse outcomes.

HIV: Re-screen at 5 months & term if high-risk behaviour mother &/or partner: STI, injected drug use, multiple partners, HIV sx. Maternal ARV tx during pregnancy & delivery, + infant ARV prophylaxis (6 wks) essential to ↓ mtct. Nausea especially bothersome with ARV; tx nausea aggressively to aid compliance (DICLECTIN ± dimenhydrinate ± metoclopramide). Plan for a scheduled cesarean section at 38 weeks if HIV RNA >1000 copies/mL near delivery.

Immunizations: P avoid live vaccines e.g. MMR, varicella. For meningococcal, use P polysaccharide. If no previous P Td immunization, a 3 dose Td schedule should be given 0, 4 weeks & 6-12 months & Tdap should replace 1 of the Td doses (Tdap should be administered ≥20 weeks gestation). Influenza: P vaccine highly recommended; tx: zanamivir RELENZA

STIs: If treating during pregnancy, retest to ensure cure. Screen during 3rd trimester in patients at high risk of acquiring a STI. If patient acquires an STI > 5 months gestation, re-screen for HIV.

Urinary Tract Infection: (see chart pg 64) cephalexin or amoxicillin x7days if sensitive; nitrofurantion x5days avoid ≥36 weeks, trimethoprim avoid 1st trimester ± sulfamethoxazole avoid last 6 weeks x 3days. **Asymptomatic Bacteriuria**: screen at 12-16 weeks gestation. Use urine culture, not leukocyte esterase or nitrate tests. See above for antibiotic options & duration. Follow-up urine culture 1 week post-treatment, & then monthly for rest of pregnancy.

Vulvovaginal Candidiasis: (see charts pg 51-53) P topical clotrimazole or miconazole x7days preferred, P topical nystatin x 14 days, F fluconazole 150mg po x 1 single, low dose treatment appears safe

Post-Partum/Lactation **Immunizations:** all vaccines L; **HIV:** L avoid breastfeeding to ↓ transmission risk (5-20% in developed countries). **Nipple 1) candidiasis**: miconazole 2% cream MICATIN; **2) fissures**: mupirocin 2% ointment BACTROBAN; **3) inflamed**: low-mid potentcy steroid (e.g. hydrocortisone). Apply after breastfeeding.[32] Infant oral candidiasis: nystatin.

Acne in Pregnancy[24] see charts pg 18, 19 — Consider non-drug & topical treatment 1st

- Topical: P L clindamycin; F L benzoyl peroxide, salicylic acid
- P isotretinoin ACCUTANE Avoid pregnancy during treatment & delay conception 1 month after stopping (counsel re: birth control); tetracyclines

Allergy, Constipation & URTI (Over-the-Counter Products) see chart pg 94

- **Antihistamine**: P L 1st generation (e.g. chlorpheniramine, diphenhydramine)
- **Constipation**: P L fiber, docusate, lactulose, senna; F L polyethylene glycol LAX-A-DAY
- **Cough**: P L dextromethorphan (DM). Avoid products with ethanol.
- **Decongestant**: P L saline nasal spray SALINEX, F L topical oxymetazoline

Asthma[25] see charts pg 112-113

- Uncontrolled asthma: ↑ risk of low birth weight, small for gestational age, preterm labour & delivery, & preeclampsia. Asthma will worsen in ~1/3 usually 2nd or 3rd trimester, & return to pre-pregnancy state within 3 months post-partum.
- Intermittent asthma: P L salbutamol
- Persistent asthma: Step 1: low dose inhaled corticosteroid, Step 2: LABA +/- medium dose inhaled corticosteroid, Step 3: LABA + high-dose corticosteroid
- P L Budesonide preferred, beclomethasone, fluticasone; P L formoterol, salmeterol

Depression & Anxiety[26] see charts pg 100,101,104-5 — Consider risk vs benefit, & risk of not treating

- Screen: pre- & post conception, & 6 weeks post-partum. Screen for thyroiditis (TSH, FT4) post-partum
- F SSRIs (see below Q&A for PAXIL), bupropion, amitriptyline, nortriptyline, desipramine; P SNRIs
- P→P benzodiazepines, F chlorpromazine,methotrimeprazine, P other antipsychotics
- St.John's Wort: Limited human data. No teratogenicity reported. Buyer beware.
- See Q&A: http://www.rxfiles.ca/rxfiles/uploads/documents/Antidepressants-PregnancyandBreastfeeding-QandA.pdf

Herbal/Natural Products[27] see charts pg 92-93 — ASK patient if using herbal products

- Generally avoid herbal products. Less safety data on the use of herbals during pregnancy/lactation than conventional medications, & not all safe or have a NPN.
- Herbals for inducing labour: F castor oil, raspberry leaf; P blue cohosh
- Herbals for increasing lactation: none are considered safe or effective
- Omega-3: F ≤2g/day, ?effectiveness. Encourage dietary sources walnuts, soybeans, salmon, etc

GERD/Heartburn in Pregnancy see charts pg 41, 95

- P Ca^{++} Carbonate TUMS, Mg^{++}, alginate antacids preferred; ranitidine
- P Omeprazole most data, lansoprazole, pantoprazole; cimetidine

Nausea & Vomiting[28] see charts pg 44-45

- P Doxylamine/pyridoxine DICLECTIN ± dimenhydrinate ± phenothiazine or ± metoclopramide. May also add on additional pyridoxine 25mg po q8h.
- F Ginger 250mg po q6h tablets – effectiveness similar to pyridoxine and dimenhydrinate. May have delayed onset (≥3 days). Buyer beware.

Pain & Fever[29] see charts pg 69-70

- P L Acetaminophen, $P_{1,3}$ L NSAIDs → ? block implantation, spontaneous abortion, malformations, prematurely closes ductus arteriosus, inhibit labour, fetal renal toxicity. Breastfeeding: ibuprofen preferred NSAID. Topical NSAIDs: likely safe. Avoid occlusive dressings.
- Opioids:[30] $P_{1,2}$ Codeine, tramadol; F for other commonly used opioids. 3rd trimester use may cause neonate depression & withdrawal. Abrupt discontinuation may cause premature labour & spontaneous abortion. Taper to lowest effective dose.
  - L Codeine – risk of morphine toxicity in ultrarapid CYP2D6 metabolizers. Limit use to 4 days. Monitor baby for limpness, difficulty breathing/feeding, or ↑ sleep.
  - L Morphine, methadone, fentanyl; L hydromorphone, oxycodone.
- Migraines:[31] migraines without aura tend to improve during pregnancy. Breastfeeding may protect against migraines. P Acetaminophen, caffeine≤300mg/day, metoclopramide - consider combining all 3 if required. F Sumatriptan IMITREX

See On-line Extras for information on Contraception, Galactagogues for Breastfeeding, & Polycystic Ovary Syndrome

A1C=hemoglobin A1C ACEI=angiotensin converting enzyme inhibitor ACR=albumin to creatinine ratio ARB=angiotensin receptor blocker ARV=antiretroviral ASA=acetylsalicylic acid BF=breastfeeding BG=blood glucose BMI=Body Mass Index CI=contraindicated CKD=chronic kidney disease DBP=diastolic blood pressure d/c=discontinue DM=diabetes mellitus dx=disease FBG=fasting blood glucose FT4=free thyroxine GDM=gestational diabetes mellitus GestHTN=gestational hypertension GFR=glomerular filtration rate HIV=human immunodeficiency virus HTN=hypertension hx=history LABA=long-acting beta agonist LT3=liothyronine LT4=levothyroxine MMI=methimazole MMR=measles, mumps, rubella mtct=mother-to-child transmission NPN=Natural Product Number NSAID=non-steroidal anti-inflammatory drug OGTT=oral glucose tolerance test PTU=propylthiouracil SOB=shortness of breath SMBG=self-monitoring blood glucose SNRI=serotonin norepinephrine receptor inhibitor SSRI=selective serotonin receptor inhibitor STI=sexually transmitted infection sx=symptom T1DM=type 1 diabetes mellitus T2DM=type 2 diabetes mellitus Td=tetanus, diphtheria Tdap=tetanus, diphtheria, pertussis TSH=thyroid stimulating hormone tx=treatment UL=upper limit

	Pre-Pregnancy (~3 months prior) &/or Potential for Pregnancy	Pregnancy — Pregnancy [P] Safe, [P] Likely Safe, [P] Caution, [P] CI, [P] Unknown	Post-Partum & Lactation — Lactation [L] Safe, [L] Likely Safe, [L] Caution, [L] CI, [L] Unknown
Activity [33]	⇨Encourage activity as part of a healthy lifestyle. ⇨Goal is ≥2.5 hours of activity/week, broken into ≥10 minute sessions. ⇨Decreases risk of pregnancy complications see Body Weight section **~ ½ of pregnancies (⅔ of diabetic pregnancies) are unplanned. Treat every patient visit with females of childbearing potential as an opportunity for preconception counseling.**	⇨PARmed-X Pregnancy Questionnaire: a screening tool for assessing safety, type & intensity of exercise during pregnancy. (http://www.csep.ca/cmfiles/publications/parq/parmed-xpreg.pdf) ⇨Recommend activities which ↓ risk of falls/fetal impact: [P] Walking, stationary cycling, swimming, low-impact aerobics [P] Running, Yoga & Pilates inform instructor, avoid compression of the abdomen & strong twists, as well as lying on back during last 4 months of pregnancy. [P] Horseback riding, skiing, hockey, gymnastics, sauna, hot tub/yoga [P] Scuba diving ⇨Stop exercising & see physician if: excessive SOB, chest pain, contractions, vaginal bleeding or gush of fluid, dizzy or faint. ⇨Targeted heart rate during pregnancy: age (beats/min) <20 (140-155), 20-29 (135-150), 30-39 (130-145), ≥40 (125-140) If **obese** (BMI ≥30kg/m²): age 20-29 (102-124), 30-39 (101-120) ⇨ "Talk test" can also be used to monitor intensity • Goal: ability to maintain a conversation while exercising	⇨ Pelvic floor exercises (i.e. **Kegel**): start immediately post-partum to ↓ risk of future stress urinary incontinence. ⇨ Assess ability to (re)start exercise at 6 week post-partum visit for both vaginal & cesarean deliveries. • May need to ↓ or limit intensity & duration of exercise. ⇨ Lactation: moderate exercise will not impact quantity or composition of breast milk. • Maximal intensity workouts: ↑ lactic acid in breast milk → ? may be less palatable to infant.

[PL] **Ca++** Total 1300mg/day ≤18 yrs, 1000mg/day ≥19 yrs; [PL] **Vitamin D** Total 600 IU/day[IOM] – 2000 IU/day[CPS], consider periodic 25(OH) level; [PL] **Vitamin A** retinol > 10,000 IU or 3000mcg/day (teratogenic)
Vitamin D deficiency risk factors: dark skin, ↓ sunlight north of 55th parallel (i.e. LaRonge, Edmonton), ↓ sun exposure (SPF≥8, institutionalized, occlusive clothes), elderly, obese, malabsorption or renal dx, medications e.g. anticonvulsants, antiretrovirals, cholestyramine, corticosteroids, rifampin

Nutrition [1,2,3,4] see chart pg 97

Pre-Pregnancy:

⇨ [P] **Folic acid: dose based on risk of neural tube defect**
- Low risk: 0.4-1mg po daily, initiate 2-3 months prior
- High risk*: folic acid 5mg po daily, initiate 3 months prior

***High risk**: family history of neural tube defect, DM, BMI >35kg/m², epilepsy, high-risk ethnic group (e.g. Sikh), malabsor[illegible] liver o[illegible] kidney dx, alcohol abuse, hemolytic anemia, medica[illegible] (anticonvulsants, methotrexate, sulfonamide, trime[illegible]

Is too much folic acid harmful? Likely not. It is a water [illegible] but it may mask vitamin B_{12} deficiency. Studies inve[illegible] potential ↑ risk of cancer are conflicting.

Calcium Supplements: Carbonate – least expensive, highest % of elemental Ca++, take with food. Citrate – less GI side effects.

Maternal Multivitamins: Generic & store brands available $4-8 (cost/month)
- MATERNA▼ [Fe++ 27mg, folic acid 1mg, Ca++ 250mg, Vit D 400IU] $8
- PregVit/PregVit folic 5 Rx✗⊗ [Fe++ 35mg, folic acid 1.1/5mg, Ca++ 300mg, Vit D 250IU]. BID: pink tab (Fe++) in am, blue tab (Ca++, folic acid) in pm. $33/$44
- PALAFER CF [Fe++ 100mg, folic acid 0.5mg] $18
- Folic acid 0.4mg OTC,✗⊗ $2, 1mg OTC,✗▼ $2, and 5mg Rx, on SPDP,▼ $8

Pregnancy:

⇨ [P] **Folic acid: dose based on risk of neural tube defect**
- Low risk: 0.4-1mg po daily throughout pregnancy
- High risk: 5mg po daily 1st trimester, then ↓ 0.4-1mg po daily

⇨ [P] **Iron:** supplem[illegible] 16-[illegible]mg elem[illegible]

[illegible]

⇨**Caloric intake**: ↑ by 340 calories/day during the 2nd trimester & by 450 calories/day during the 3rd trimester. 2-3 extra Food Guide servings per day are all that is needed (e.g. 1 large glass of milk & 1 piece of fruit). Health Canada Pregnancy Good Guide Serving Tracker available on-line

Post-Partum & Lactation:

⇨ [L] Folic acid: continue 6 weeks post-partum or as long a breastfeeding continues.

⇨ **Vitamin D** for term infants dur[illegible] 1st y[illegible] [illegible]00 IU/day, or 800 IU/[illegible]

[illegible] 200 [illegible]/kg/day (max 400 IU/day). See RxFiles Vitamin D Q&A: http://www.rxfiles.ca/rxfiles/uploads/documents/Vitamin-D-Overview-QandA.pdf

⇨ Fe++ (iron-rich food/cereals, supplements) in breastfed infants ≥4-6 mos

⇨ **Caloric intake during lactation:** ↑ by 330 calories/day 0-6 months postpartum, & ↑by 400 calories/day 7-12 months post-partum.

Fish & Mercury Levels during Pregnancy & Breastfeeding: Health Canada recommends 2 servings of fish/week (75g=2.5oz=½ cup). Limit fish with high mercury levels (fresh/frozen tuna, shark, swordfish, marlin, orange roughy, escolar) to 150g/month. Limit canned albacore (white) tuna to 300g/week.[34] Refer to Health Canada's Food Safety for Pregnancy Women for information on other foods to avoid (e.g. certain cheeses, deli meats, etc) http://www.hc-sc.gc.ca/hl-vs/alt_formats/pdf/iyh-vsv/food-aliment/pregnant-enceintes-mar-2010-eng.pdf

Full chart available to online subscribers at RxFiles.ca!

Body Weight [35]

Pre-Pregnancy:

⇨Encourage BMI <30kg/m² (ideal 18.5-24.9kg/m²). Promote diet & exercise to ↓ weight. If obese, start folic acid 5mg OD.
⇨Screen: diabetes (i.e. FBG, A1C)
⇨Pregnancy complications with BMI >30kg/m² include:
- ↑ risk of infertility, cesarean section, stillbirth & blood clots
- 2-fold increase in neural tube defects, and ↑ risk of other malformations
- Miscarriage — Odds Ratio (OR) 3.5 (95% CI 1.03-12.01)
- Spontaneous abortion — OR 1.2 (95% CI 1.01-1.46)
- Hypertension — OR 3.0 (95% CI 2.29-2.62)
- Gestational diabetes — OR 2.6 (95% CI 2.1-3.4)
- Large infant birth weight (>4500g) — OR 2.0 (95% CI 1.4-3)

Pregnancy:

Pre-pregnancy BMI[36]	**Rate** of weight gain (mean) 2nd & 3rd trimester kg (lb)/week	**Total** weight gain kg (lb) (based on ≤2kg (4.4lb) weight gain in 1st trimester)
<18.5	0.5 (1)	12.5-18 (28-40)
18.5-24.9	0.4 (1)	11.5-16 (25-35)
25-29.9	0.3 (0.6)	7-11.5 (15-25)
≥30	0.2 (0.5)	5-9 (11-20)

⇨Ultrasound to assess anatomic structures: if obese, consider scheduling at 20-22 weeks as obesity ↓ visibility of structures.

Post-Partum & Lactation:

⇨Lactation: obesity has been linked to breastfeeding challenges such as ↓ prolactin response and delayed lactogenesis.
- Refer mother to a Lactation Consultant if she is experiencing difficulties with breastfeeding (e.g. LaLeche League www.lllc.ca)

⇨Breastfeeding promotes postpartum weight loss. Breastfeeding burns 500-600 calories/day.

Alcohol [37]

- ♦ No safe amount has been identified; studies searching for a threshold are conflicting.
- ♦ Abstinence is the safest choice. Fetal Alcohol Syndrome (FAS) occurs with prolonged heavy drinking.
- ♦ Some alcohol ingestion prior to knowledge of pregnancy is unlikely to cause harm.
- ♦ Hold breastfeeding ≥2 hours/drink to avoid infant exposure to alcohol. Monitor infant for sedation & impaired motor skills. Alcohol may ↓ milk production & alter taste of milk ↓ infant milk ingestion.

Caffeine [38]

- ♦ Ok if ≤300mg/day (~2 x 8oz cups of coffee) during pre-conception, pregnancy & breastfeeding

Smoking [39] see chart pg 115 — Ask, Advise, Assess, Assist & Arrange

- ♦ [PL] Tobacco – avoid maternal & second-hand smoke during pregnancy as it ↑ risk fetal/infant morbidity & mortality. Smoking during lactation ↓ milk production & ↑ risk of infant colic.
- ♦ **Smoking cessation**: 1st line – counseling; success rates with high vs low intensity were non-significant. Advise at minimum.
  - 2nd line - [PL] nicotine replacement therapy (NRT). Gum & lozenge ↓ exposure, as does limiting the patch to 16 hours/day. ↑metabolism of nicotine during 3rd trimester – may require ↑ in NRT doses.
  - Other options: [PL] nortriptyline; [PL] buproprion. May be preferred in patients with comorbidities (e.g. depression).

Contraction [40] see charts pg 86-88

Pre-pregnancy:

⇨After stopping hormonal contraception, fertility is restored in:
- 1-3 months with combined oral contraceptives
- 9 months (range 4-11) with medroxyprogesterone DEPO-PROVERA. Rate of conception after the last injection is 50% at 10 months, & 90% at 24 months.

⇨Intrauterine device (IUD) MIRENA, NOVA-T does not ↑ risk of infertility

Pregnancy: IUD does not ↑ risk of ectopic pregnancy. However, if conception occurs while an IUD is inserted, assess for an ectopic pregnancy.

Post-Partum/Lactation:

⇨Lactational amenorr [illegible] returned, 2) almost e [illegible] ≤4h during the day & [illegible]

⇨ Progestin-only products often preferred post-partum as there is no impact on lactation. The oral contraceptive pill MICRONOR (taken every day, no pill-free interval), injection DEPO-PROVERA & implant IMPLANON (US only) can be started immediately after delivery as a contraceptive, ±breastfeeding. Wait 6 weeks post-partum before inserting an IUD MIRENA; may be inserted immediately if cesarean.

⇨ There is insufficient evidence to determine if combined oral contraceptives impact the quality & quantity of breast milk.

⇨ L Avoid combined oral contraceptive pills during the first 3 weeks post-partum. Avoid during the first 6 weeks IF at risk of venous thromboembolism (VTE) age≥35, smoker, thrombophilia, immobility, previous VTE, preeclampsia, recent cesarean, BMI ≥30kg/m^2, post-partum hemorrhage.

Galactagogues for Breastfeeding [41]

⇨Medications should never replace support, education & assessment of breastfeeding technique.

⇨Frequent feeds & complete milk removal at regular intervals will increase milk production.

⇨There is insufficient evidence to recommend the use of pharmacologic or herbal galactagogues. Trials investigating domperidone & metoclopramide were primarily of poor quality, small numbers ≤50 patients, short duration ≤4 weeks, & had high-drop out rates.

⇨There is no evidence that ↑ prolactin levels equate to ↑ milk production.

⇨Anecdotally, medications may be of some benefit in adoptive mothers who wish to breastfeed, to re-establish breastfeeding after weaning, or mothers of babies in neonatal intensive care. Refer other mothers experiencing difficulties with breastfeeding to a Lactation Consultant before trialing drug therapy (e.g. LaLeche League www.lllc.ca).

⇨Domperidone MOTILIUM 10mg po TID [max 60mg/day]. There is no evidence that doses >30mg/day are more effective, & risk of side effects ↑ (e.g. QT prolongation). May take up to 4 days for improvement. Trial for 6 weeks. Taper by ↓ 1 pill q4-7 days. Preferred over metoclopramide due to ↓ side effects.

⇨Metoclopramide MAXERAN 10mg po TID-QID x 7-14 days, then taper by ↓ 1 pill q5-7 days.

⇨Herbals: even less data than prescription galactagogues. Several herbal galactagogues are not recommended during breastfeeding (e.g. fenugreek, blessed thistle, fennel, caraway, Goat's rue).

⇨Beer: the barley component of beer may ↑ prolactin, but there is insufficient evidence to recommend & alcohol may ↓ milk production.

⇨Bromocriptine PARLODEL is not recommended for the suppression of lactation due to an ↑ risk of stroke and myocardial infarctions when used postpartum.

Polycystic Ovary Syndrome (PCOS) [42] Up to 74% of PCOS females experience infertility

⇨↑ risk of pregnancy complications: gestational diabetes, HTN, preeclampsia, and neural tube defects if obese & pre-existing DM. Use folic acid 5mg po daily if trying to conceive, or if on metformin & sexually active.

⇨1st line: Weight loss via diet & exercise (if obese); a ↓ in body weight of 5-10% can restore ovulation.

⇨**Clomiphene** CLOMID: **1st line for drug-induced ovulation**
- Dose: 50mg [illegible] daily x 5 days (s [illegible]). If pregnancy does not occur, repeat. If [illegible] ccur, ↑ to 100mg /day.
- [illegible] g. Consider ineffective if [illegible] 3 cycles of maximum dose. Limit to 12 cycles (↑ risk of ovarian tumours).
- Precautions: ↑ rate of twins (~8%) and triplets (0.3%), hot flashes (>10%), visual blurring/after images (≤2%).

⇨ **Metformin: 2nd line as adjuvant (off-label indication)**
- Versus placebo, metformin ↑ ovulation rates but non-significant for pregnancy rates. However, anecdotally, some PCOS patients do become pregnant shortly after starting metformin.
- Consider adding it to clomiphene in clomiphene-resistant patients who are older & have visceral obesity.
- Dose: start 250-500mg po daily with food. Titrate up q2weeks to 750-850mg po TID as tolerated.
- Lack of evidence to support continued metformin use during pregnancy; however, likely safe.

⇨**Other options**: referral for gonadotropin injections, ovarian drilling (laparoscopic procedure in which the ovary is punctured leading to less testosterone production), in vitro fertilization.

Hypertension in Pregnancy [7]

- Types of Hypertension during Pregnancy:
  - **Pre-existing HTN**: HTN diagnosed prior to conception or before 20 weeks gestation
  - **Pre-existing HTN + Preeclampsia**: occurs after 20 weeks gestation with the following:
    - resistant HTN (≥3 antihypertensive drugs), or new or worsening proteinuria, or ≥1 adverse condition*
  - **Gestational HTN:** HTN diagnosed ≥20 weeks
  - **Gestational HTN + Preeclampsia:** new onset proteinuria, or ≥1 adverse condition*
  - **Blood pressure targets:** no comorbidities 130-155/80-105mmHg, with comorbidities (diabetes, renal disease, cerebrovascular disease) 130-139/80-89mmHg. May also consider:
    - Pre-existing HTN: consider SBP 130-140mmHg
    - Gestational HTN: consider SBP 140-150mmHg

* Table: Adverse Conditions Pertaining to Preeclampsia
Maternal Symptoms: Persistent/new/unusual headache, visual disturbances, persistent abdominal or right upper quadrant pain, severe nausea or vomiting, chest pain or dyspnea.
Maternal Signs of End-Organ Damage: Eclampsia, severe hypertension, pulmonary edema, suspected placental abruption, seizures.
Abnormal Maternal Laboratory Tests: ↑ SCr, AST, ALT, or LDH with symptoms; ↓ platelets or albumin
Fetal Morbidity

  - Defining the type of HTN is important for non-BP management & follow-up screening during pregnancy & post-partum. However, blood pressure targets are similar and antihypertensive therapy is the same regardless of type.
- Supplements for the prevention of preeclampsia:
  - Fish oils: supplements (e.g. evening primrose) have not been shown to ↓ risk of preeclampsia. P Watch mercury levels in dietary fish (see Extras). Evening primrose may delay rupture of membranes, augment oxytocin, etc.
  - P Vitamin E & C: does not ↓ risk of preeclampsia; may ↑ risk of GestHTN and premature rupture of membranes.

Full chart available to online subscribers at RxFiles.ca!

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