Therapeutic Considerations in Pregnancy

Pharmacokinetic Changes During Pregnancy

- **Normal physiologic changes that occur during pregnancy may alter medication effects, resulting in the need to monitor or adjust therapy.**
- **Physiologic changes begin in the first trimester and peak during the second.**
- **Maternal plasma volume, cardiac output and GFR increase by 30-50%, lowering the concentration of drugs excreted by the kidney.**

Drugs in Pregnancy, Fetus, Newborn

- **Therefore, pregnant women may have different drug pharmacokinetics than non-pregnant women.**
- **As fat increases during pregnancy, the volume of distribution of fat-soluble drugs increases.**
- **Plasma albumin concentration decreases, which increases the volume of distribution of highly protein-bound drugs.**

Pharmacokinetic Changes During Pregnancy

- **Unbound drug is also rapidly eliminated by liver or kidney.**
- **Hepatic perfusion increases, which may increase hepatic extraction of drugs.**
- **Nausea and vomiting as well as delayed gastric emptying may alter drug absorption.**
- **Pregnancy-induced increases in gastric pH may affect absorption of weak acids and basis.**
- **High levels of estrogen and progesterone may affect hepatic enzyme activity.**

Pregnancy-Influenced Issues

- **Pregnancy causes or exacerbate conditions that pregnant women experience: constipation, gastro-esophageal reflux, hemorrhoids, nausea and vomiting.**
- **Gestational diabetes, gestational hypertension, and venous thrombo-embolism have the potential to cause adverse pregnancy consequences.**

Pregnancy-Influenced Issues

1. **GIT:**

- **Constipation is prevalent during pregnancy, and can exacerbate hemorrhoids.**
- **Management of constipation starts first with moderate physical exercise and increased dietary intake of fibers and fluids.**
- **If additional treatment is needed. Supplemental fiber and/or stool softner is appropriate.**

Pregnancy-Influenced Issues

- **Bulk-forming agents (psyllium, methylcellulose, and polycarbophil) are safe for long-term use because they are not absorbed.**
- **Osmotic laxative (polyethylene glycol, lactulose, and sorbitol) and stimulant laxatives (senna and bisacodyl) can be used.**
- **Use of magnesium and sodium salts may cause electrolyte imbalance.**

Pregnancy-Influenced Issues

- **Castor oil and mineral oil should be avoided because they cause stimulation of uterine contractions, and impairment of fat-soluble vitamin absorption, respectively.**
- **Hemorrhoides should be treated conservatively.**

Pregnancy-Influenced Issues

- **Management of gastro-esophageal reflux disease include:**
- **Life-style and dietary modification (small frequent meals, alcohol and tobacco avoidance, food avoidance before bedtime, elevation of the head of the bed).**
- **If symptoms are not relieved, antacids (aluminum, calcium or magnesium preparations) and sucralfate are acceptable.**

Pregnancy-Influenced Issues

- **Sodium bicarbonate and magnesium trisilicate should be avoided.**
- **If the patient does not respond, histamine H_2-receptor blockers (ranitidine and cimetidine) can be used.**
- **Proton pump inhibitors (omeprazole) may not be associated with increased risk of major birth defects.**

Pregnancy-Influenced Issues

- **Nausea and vomiting of pregnancy affect ~90% of pregnant women.**
- **It begins within 4-6 weeks of gestation, peeks between weeks 8-12 and resolves by 16-20 weeks.**
- **Hyperemesis gravidarum (severe vomiting causing weight loss, dehydration, electrolyte imbalance, and ketonuria) occurs in 0.5-2% of women.**

Pregnancy-Influenced Issues

- **Dietary modifications such as eating frequent small bland meals, and avoiding fatty and spicy meals may be helpful.**
- **Ginger is effective and probably safe.**
- **Pyridoxine (vitamin B_6) and/or antihistamines (doxylamine) are effective and are first-line agents.**

Pregnancy-Influenced Issues

- **Metoclopramide and phenothiazines may cause sedation and extrapyramidal effects including dystonia (but can be used).**
- **Ondansetron (serotonin 5-HT_3 receptor antagonist) is controversial and may cause oral clefts.**
- **Corticosteroids may be effective. Reserved for use after the first trimester, because of risk of oral clefts.**

Pregnancy-Influenced Issues

2. Gestational diabetes (GDM):

- **GDM is diabetes diagnosed during the second and third trimester.**
- **It develops in 3-5% of pregnant women.**
- **Risks of GDM include fetal loss, increased risk of congenital malformations, and macrosomia.**
- **Nutritional education with dietary modifications, exercise and blood glucose monitoring are considered first-line for all women with GDM.**

Pregnancy-Influenced Issues

- **85% of patients can achieve control with this first line therapy.**
- **Human insulin is the drug of choice for GDM because it does not cross the placenta.**
- **Glyburide and metformin are alternatives but long-term safety data are limited.**

Pregnancy-Influenced Issues

3. **Hypertensive disorders of pregnancy:**

- **Complicate ~ 10% of pregnancies.**
- **Include:**

a. **Preeclampsia-eclampsia.**

b. **Chronic hypertension (preexisting hypertension or developing before 20 weeks of gestation).**

c. **Chronic hypertension with superimposed preeclampsia.**

Pregnancy-Influenced Issues

d. **Gestational hypertension (without proteinuria developing after 20 weeks of gestation).**

- **Defined as hypertension > 140/90.**
- **Nondrug management: activity restriction (?), stress reduction, and exercise. Prolonged bed rest may increase the risk of venous thromboembolism.**

Pregnancy-Influenced Issues

- **Use of supplemental calcium 1-2 g per day decreases the risk of hypertension and preeclampsia in patients with initial low calcium intake, but not in those with adequate calcium intake.**
- **Antihypertensive drugs will be discussed later in this lecture.**

Pregnancy-Influenced Issues

Preeclampsia:

- **Develops after 20 weeks of gestation.**
- **Chronic and gestational hypertension may be complicated with preeclampsia.**
- **It is a multisystem syndrome: renal failure, maternal morbidity/mortality, preterm delivery, and intrauterine growth retardation.**

Pregnancy-Influenced Issues

- **Treatment: in addition to treatment of hypertension, low-dose aspirin 60-81 mg/day beginning late in the first trimester in women at risk of preeclampsia.**
- **The only cure is delivery of the placenta.**

Pregnancy-Influenced Issues

Eclampsia:

- **Seizures on top of preeclampsia.**
- **It is a medical emergency.**
- **May be prevented by low dose aspirin.**
- **Magnesium sulfate is effective in preventing eclampsia and treating its seizures.**
- **Usual dose 4-6 g IV over 15-20 min, followed by 2g/hr continuous IV infusion for 24 hours.**
- **Diazepam and phenytoin should be avoided.**

Pregnancy-Influenced Issues

4. **Venous Thrombo-embolism (VTE):**

- **Risk of VTE in pregnant women is 5-10 fold higher than that in non-pregnant women.**
- **Low-molecular-weight heparin (LMWH) is preferred over unfractionated heparin (UFH) for treatment of acute VTE in pregnancy.**
  Treatment should be continued throughout pregnancy and for 6 weeks after delivery (minimum duration of therapy should not be < 3 months).

Pregnancy-Influenced Issues

- **Fondaparinux (synthetic pentasaccharide) and injectable direct thrombin inhibitors (lepirudin, bivalirudin) should be avoided unless the patient has heparin-induced thrombocytopenia.**
- **The oral agents dabigatran (direct thrombin inhibitor), rivaroxaban (direct factor Xa inhibitor), apixapan (direct factor Xa inhibitor) are not recommended.**

Pregnancy-Influenced Issues

- **Warfarin should not be used because it causes nasal hypoplasia, stippled epiphysis, limp hypoplasia, and eye abnormalities (risk period 6-12 weeks of gestation). CNS anomalies are associated with exposure during 2nd and 3rd trimesters.**

Pregnancy-Influenced Issues

- **In women with high risk for VTE, antipartum LMWH prophylaxis, with 6 weeks postpartum prophylaxis with LMWH or warfarin is recommended.**
- **Women with prosthetic heart valves should receive LMWH twice daily (or UFH every 12 hours) during pregnancy.**
- **LMWH should be adjusted to achieve a peak anti-Xa level at 4 hour post-subcutaneous dose.**

Pregnancy-Influenced Issues

- UFH treatment should target a mid-interval aPTT value at least twice the control value or an anti-Xa level of 0.35-0.7 units/mL.
- High risk women with prosthetic heart valves may also receive low-dose aspirin of 75-100 mg/day.

Acute Care Issues in Pregnancy

1. **Urinary Tract Infections (UTIs):**

- ***Escherichia coli* is the primary cause of infection in 75-90 % of cases.**
- **Other gram-negative rods (*Proteus* and *Klebsiella*), as well as, group B *Streptococcus* (GBS) account for some infections.**
- **The presence of GBS in urine indicates heavy colonization of the genitourinary tract, increasing the risk for GBS infection in the newborn.**

Acute Care Issues in Pregnancy

- **UTIs are asymptomatic (asymptomatic bacteriuria) or symptomatic (cystitis and pyelonephritis).**
- **Treatment of asymptomatic bacteriuria and cystitis is necessary to prevent pyelonephritis. Duration of treatment 7-14 days.**
- **The most commonly used antibiotics to treat asymptomatic bacteriuria and cystitis are β-lactam antibiotics [peniclillins (amoxacillin)and cephalosporins] and nitrofurantoin.**

Acute Care Issues in Pregnancy

- **β-lactam antibiotics are not teratogenic, but *E. coli* resistance to ampicillin and amoxicillin limits their use as single agents.**
- **Nitrofurantoin is not active against *Proteus* species and should not be used after week 37 in patients with G6PD deficiency because of the risk of hemolytic anemia in the newborn.**
- **Sulfa-containing drugs (co-trimoxazole) can contribute to the development of newborn kernicterus, and should be avoided during the last week of gestation.**

Acute Care Issues in Pregnancy

- **Trimethoprim is a folate antagonist that is contraindicated during the first trimester because of association with cardiovascular malformations.**
- **Fluoroquinolones are containdicated because of association with impaired cartilage development.**
- **Tetracyclines are containdicated because of association with deciduous teeth discoloration, if given after 5 months of gestation.**

Acute Care Issues in Pregnancy

- **Pyelonephritis is more severe and is associated with premature delivery, low infant birth weight, hypertension, anemia, bacteremia, and transient renal failure.**
- **Hospitalization is the standard of care for pregnant women with pyelonephritis.**
- **Therapy include parenteral administration of 2nd and 3rd generation cephalosporins (cefuroxime and ceftriaxone), ampicillin + gentamicin, or ampicillin-sulbactam.**

Acute Care Issues in Pregnancy

- **Switching to oral therapy is likely if the woman is afebrile for 48 hours.**
- **The total duration of therapy for acute pyelonephritis is 10-14 days.**
- **Nitrofurantoin should be avoided because it does not achieve therapeutic levels outside urine.**

Acute Care Issues in Pregnancy

2. Sexually transmitted Infections (STIs):

- **Can be classified as:**

a. **Infections that may be transmitted across the placenta and infect the infant prenatally (syphilis).**

b. **Infections that can be transmitted during birth and cause neonatal infections (*Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Herpes simplex virus*).**

Acute Care Issues in Pregnancy

c. **Infections that pose a threat for preterm labor (bacterial vaginosis, BV).**

- **Treatment for some sexually transmitted diseases in pregnancy is shown in the following table.**

STI	Drug Name (Brand Name)	Usual Dose	Monitoring	Comments
Bacterial vaginosis	*Recommended:* • Metronidazole (Flagyl) ***OR*** • Metronidazole 0.75% gel *Alternatives[a]:* Clindamycin (Cleocin)	500 mg by mouth two times daily × 7 days 5 g intravaginally once daily × 5 days	Follow-up testing not required if symptoms resolve	No link between intravaginal clindamycin and newborn complications Oral or vaginal preparations can be used
Chlamydia	*Recommended:* Azithromycin (Zithromax) *Alternatives[a]:* Amoxicillin (Amoxil) Erythromycin base Erythromycin ethylsuccinate	1 g by mouth × 1 dose	Test-of-cure at 3-4 weeks after therapy completion; retest all after 3 months	Gonorrheal coinfection common; both are treated concurrently Chlamydia is asymptomatic in men and women Women below age 25 years and those at high risk should be retested in the third trimester

Genital herpes	*Recommended:* Acyclovir (Zovirax) ***OR*** Valacyclovir	400 mg by mouth three times a day 500 mg by mouth twice a day	Routine serologic testing for HSV-2 is not recommended	Start treatment at 36 weeks of gestation
Gonorrhea	*Recommended:* Ceftriaxone (Rocephin) *PLUS* Azithromycin (Zithromax)	250 mg IM × 1 dose 1 g by mouth × 1 dose	Because of high reinfection rate, repeat testing for gonorrhea 3 months after treatment	Chlamydial coinfection common; both are treated concurrently Consult with infectious disease specialist if cephalosporin allergy
Trichomoniasis	*Recommended:* Metronidazole	2 g by mouth × 1 dose	Rescreen HIV patients at 3 months after treatment	While tinidazole is an alternative for nonpregnant women, avoid during pregnancy

Syphilis[b]				
Primary, secondary, early latent	*Recommended:* Benzathine penicillin G (Bicillin L-A)	2.4 million units IM × 1 dose; a second dose can be given 1 week after initial dose	Nontreponemal serologic evaluation[c] at 6 and 12 months	For treatment failure or reinfection, use same drug and dose but increase to 3 weekly doses unless neurosyphilis is present
Tertiary, late latent	*Recommended:* Benzathine penicillin G (Bicillin L-A)	2.4 million units IM × 3 doses at 1-week intervals	Nontreponemal serologic evaluation[c] at 6, 12, and 24 months. CSF examination may be required	Use this regimen for late latent or latent syphilis of unknown duration
Neurosyphilis	*Recommended:* Aqueous penicillin G (Pfizerpen) *Alternative[a]:* Procaine penicillin (Wycillin, Pfizerpen-AS) *PLUS* Probenecid	3–4 million units IV every 4 hours or 18–24 million units IV continuously × 10–14 days 2.4 million units IM daily × 10–14 days 500 mg by mouth four times daily × 10–14 days	If initial elevation of leukocytes in CSF, repeat CSF examination every 6 months until normalization	Consider repeat treatment if CSF leukocytes or protein do not normalize after 2 years Use alternative regimen only if compliance can be ensured

Acute Care Issues in Pregnancy

3. **Headache:**

a. **Primary headaches : tension and migraine.**

b. **Secondary headaches: those caused by eclampsia, stroke, postdural puncture, cerebral angiopathy, and cerebral venous thrombosis.**

- **Migraine headaches are associated with estrogen fluctuations in women of child-bearing age.**

Acute Care Issues in Pregnancy

- **60-70% of pregnant women with a history of migraine headaches experience improvement during pregnancy.**
- **20% experience complete cessation.**
- **Improvement is more likely in women who have migraine without aura and in women who have a history of menstrual migraine.**

Acute Care Issues in Pregnancy

- **Tension headaches are les studied. Most women report no change in frequency or intensity.**
- **Relaxation, stress management, and biofeedback are all effective non-pharmacological treatments, with minimal risk.**
- **For tension headaches acetaminophen or ibuprofen can be used.**

Acute Care Issues in Pregnancy

- While ibuprofen is considered safe, all NSAIDs are contraindicated in the third trimester because of the danger of premature closure of the ductus arteriosus.
- Aspirin should also be avoided in the third trimester because in addition to that, it can cause maternal and fetal bleeding as well as decreased uterine contractility (prolonged labor).

Acute Care Issues in Pregnancy

- For migraine headaches analgesics (acetaminophen and ibuprofen) are indicated.
- Opioids may contribute to migraine-associated nausea, and long-term use near term can cause neonatal withdrawal.
- For non-responsive migraine, sumatriptan can be used (other triptans lack information about use in pregnancy).
- Ergotamines are contraindicated because of effects on uterine tone.

Acute Care Issues in Pregnancy

- **Promethazine, prochlorperazine, metoclopramide may be used for patients with migraine associated nausea.**
- **Propranolol (given at the lowest effective dose) and amitrptyline (10-25mg PO daily) can be used for prophylaxis in patients who experience severe migraine.**

Chronic Illnesses in Pregnancy

Treatment of Chronic Illnesses in Pregnancy

Chronic Illness	Treatment	Comments
Allergic rhinitis	Intranasal corticosteroids Intranasal cromolyn First generation antihistamines (chlorpheniramine, diphenhydramine, hydroxyzine)	Budesonide and beclomethasone most widely studied intranasal corticosteroids Second generation antihistamines do not appear to increase fetal risk, but are less extensively studied than first generation products Use of external nasal dilator, short-term topical oxymetazoline, or ICS may be preferable to oral decongestants

Asthma Step 1 (intermittent) Step 2 and above (persistent)	SABA (albuterol) SABA (albuterol) Step-appropriate ICS LABA	Budesonide is the preferred ICS, but any may be used Alternatives are cromolyn (less effective), leukotriene receptor antagonists (less experience in pregnancy), and theophylline (more potential toxicity) Systemic corticosteroids recommended to gain control in patients with most severe disease
Epilepsy	Probably Safest AEDs • Carbamazepine • Lamotrigine • Levetiracetam • Phenytoin Lower risk than VPA • Gabapentin • Oxcarbazepine • Zonisamide Significant risk greater than other AEDs • Phenobarbital • Topiramate • VPA	Polytherapy carries higher risk of major malformations than monotherapy Rates of major malformation with probably safest AEDs clusters around 2-2.5% Phenytoin, lamotrigine, and carbamazepine may cause cleft palate Phenobarbital is associated with cardiac malformations Risk for most AED-associated malformations is dose-related Emerging evidence suggests risk of structural teratogenesis with levetiracetam is low

Chronic Illness	Treatment	Comments
HIV	Currently receiving ART: Continue current regimen if viral load is suppressed AR -naïve, no evidence of resistance: • Dual NRTI backbone ***PLUS*** • Ritonavir-boosted PI ***OR*** • NNRTI ***OR*** • Integrase inhibitor	In women currently receiving ART, antiretroviral drug resistance testing should be performed to guide ART If efavirenz is part of current ART, continue use since NTDs usually occur through weeks 5-6 of gestation and pregnancy often is not recognized during that time period If ART-naïve, any regimen containing efavirenz should be initiated after first 8 weeks of pregnancy

Hypertension, chronic	Initial treatment: Labetalol Nifedipine Methyldopa	ACE inhibitors, ARBs, renin inhibitors, mineralocorticoid receptor antagonists are not recommended Atenolol has been associated with fetal growth restriction Thiazide diuretics theoretically lower the increase in plasma volume during pregnancy, but are considered second-line
Thyroid disorders	Hypothyroid Levothyroxine Hyperthyroid • PTU • Methimazole	For hypothyroidism, attain a TSH of 0.1-2.5, 0.2-3, and 0.3-3 milli-international units/L (mIU/L) in the first, second, and third trimester, respectively Use PTU in first trimester followed by switch to methimazole in second and third trimester to balance the risk of PTU-induced hepatotoxicity and methimazole embryopathy

ACE, angiotensin converting enzyme, AED, antiepileptic drug; ARB, angiotensin receptor blocker; ART, antiretroviral therapy; ICS, inhaled corticosteroid; LABA, long-acting beta agonist; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NTD, neural tube defects; PI, protease inhibitor; PTU, propylthiouracil; SABA, short-acting beta agonist; TSH, thyroid stimulating hormone; VPA, valproic acid.

Chronic Illnesses in Pregnancy

1. **Allergic Rhinitis and Asthma:**

- **Health consequences of untreated or poorly treated asthma include: preterm labor, preeclampsia, intrauterine growth retardation, premature birth, low birth weight, and stillbirth.**
- **Risks of medications use to the fetus are less than risks of untreated asthma.**
- **Treatment strategies for allergic rhinitis in pregnancy are similar to non-pregnant women: avoidance of allergen, immunotherapy, and pharmacotherapy.**

Chronic Illnesses in Pregnancy

2. Diabetes Mellitus:

- Poorly controlled diabetes can cause fetal malformations, fetal loss, and maternal morbidity.
- Women with diabetes should use effective contraception until optimal glycemic control is achieved before attempting pregnancy.
- Human insulin is safe during pregnancy.
- Alternative for type 2 DM include metformin and glyburide.

Chronic Illnesses in Pregnancy

3. Epilepsy:

- **Seizure frequency does not change for <u>most</u> pregnant women with epilepsy.**
- **Seizures may become more frequent because of changes in maternal hormones, sleep deprivation, and medication adherence problems because of fear of teratogenic risk.**

Chronic Illnesses in Pregnancy

- **Another potential cause is changes of free serum concentration of antiepileptic drugs resulting from increased maternal volume of distribution, decreased protein binding from hypoalbuminemia, increased hepatic drug metabolism, and increased renal drug clearance.**
- **Dose adjustment should be based on the patient's clinical condition and her free serum concentration (?)of the antiepileptic drug.**

Chronic Illnesses in Pregnancy

- **The risks of uncontrolled seizures to the infant are greater than those associated with antiepileptic drugs. (especially for tonic-clonic seizures).**
- **Major malformations are 2-3 times more likely to occur in children born to women taking antiepileptic drugs than to those who do not.**
- **Use of valproic acids should be avoided during pregnancy.**

Chronic Illnesses in Pregnancy

- **Major malformations with valproic acid are dose-related and range from 6-9%.**
- **Include neural tube defects (spina bifida), facial clefts and cognitive teratogenicity.**
- **Antiepileptic drug monotherapy is recommended with dose optimized before conception.**
- **If treatment fail, valproic acid or phenobarbital can be used at the lowest effective dose (??).**

Chronic Illnesses in Pregnancy

- **All women taking antiepileptic drugs should receive folic acid supplementation (4-5 mg daily) starting before pregnancy and continuing at least through the first trimester, and preferably throughout pregnancy.**
- **Important !!**

Chronic Illnesses in Pregnancy

4. Hypertension:

- A physiologic decrease in blood pressure occurs during the first part of pregnancy reaching lowest point between 16-18 weeks of gestation.
- By the third trimester, blood pressure returns to pre-pregnancy levels.

Chronic Illnesses in Pregnancy

Chronic hypertension of pregnancy:

- **Defined as hypertension occurring before 20 weeks of gestation, the use of antihypertensive medications before pregnancy, or the persistence of hypertension beyond 12 weeks postpartum.**
- **It is classified as:**

a. **Mild/nonsevere: 140-159/90-109 mmHg**

b. **Severe: >160/<110 mmHg**

Chronic Illnesses in Pregnancy

- **Chronic hypertension can cause fetal growth restriction, maternal complications and hospital admissions.**
- **When treating chronic hypertension in pregnant women we should be careful not compromise utero-placental blood flow. Lower BP over a period of hours.**
- **If there is no end organ damage, we may not use antihypertensive drugs to treat non-severe hypertension. (<160/<105 mmHg).**

Chronic Illnesses in Pregnancy

- **When using antihypertensive medication sustain blood pressure at 120-160 / 80-105 mmHg.**

Drugs:

- **Initial choice include methyldopa, hydralazine, or labetelol.**
- **Oral nifedipine may be used.**
- **Magnesium sulfate when preeclampsia is present.**

Chronic Illnesses in Pregnancy

5. Mental health conditions:

- **Most women with mental health conditions discontinue or refuse treatment because of concern about teratogenicity, or because of paranoid or delusional thinking.**
- **In general, monotherapy is preferred over polytherapy, even if higher doses are required.**

Chronic Illnesses in Pregnancy

A. Depression:

- **Maternal depression is associated with greater risk for premature birth, low birth weight, miscarriage, and fetal growth restriction, and long-term implications for normal infant development.**
- **SSRIs (paroxetine) are not considered major teratogens, and are relatively safe.**
- **Risks with SNRIs are less defined.**

Chronic Illnesses in Pregnancy

- Use of SSRIs, SNRIs, and TCAs in the later part of pregnancy is associated with persistent pulmonary hypertension of the newborn, and "Prenatal Antidepressant Exposure Syndrome" (cardiac, respiratory, neurological, GI, and metabolic complications from drug toxicity or withdrawal of drug therapy).
- Women who stop taking antidepressants are more likely to relapse, which have negative implications on the well being of the fetus.

Chronic Illnesses in Pregnancy

Benzodiazepines:

- The use of diazepam during pregnancy is associated with increased risk of oral clefts.
- Benzodiazepines used in the third trimester can cause infant sedation and withdrawal symptoms (restlessness, hypertonia, hyperreflexia, tremulousness, apnea, diarrhea and vomiting).
- "Floppy-Baby Syndrome" has also been described (low Apgar scores, hypothermia, poor muscle tone, feeding difficulties, and poor temperature adaptation).

Chronic Illnesses in Pregnancy

Mood Stabilizers:

- **Commonly used drugs are lithium, lamotrigine, carbamazepine, and valproic acid.**
- **Lithium use for bipolar disorders during pregnancy was associated with increased risk of cardiac malformations (especially Ebstein's anomaly, which involves the tricuspid valve).**
- **Other neonatal adverse effects include floppy baby syndrome, nephrogenic diabetes insipidus, hypoglycemia, cardiac arrhythmias, thyrpoid dysfunction, polyhydramnios, and premature delivery.**

Chronic Illnesses in Pregnancy

- **Lithium level, thyroid and renal functions should be monitored during pregnancy.**
- **Lithium may cause lethargy, hypotonia, hypothermia, cyanosis, and changes in ECG in breastfed infants.**
- **In breastfeeding, lithium level, thyroid functions and CBC should be monitored.**

Chronic Illnesses in Pregnancy

B. Schizophrenia:

- **Maternal schizophrenia is associated with increased risk of perinatal death, low birth weight, small-for-gestational-age infants, cardiovascular malformation, pre-term delivery, stillbirth, and infant death.**
- **Both the typical and the atypical antipsychotics were not adequately evaluated for use during pregnancy.**

Chronic Illnesses in Pregnancy

- **The typical antipsychotics (chlorpromazine, haloperidol, and perphenazine) were used during pregnancy with no reported congenital malformations.**
- **Atypical antipsychotics (olanzapine, clozapine, quetiapine, and resperidone) use during pregnancy showed a higher rate of low-birth-weight, and cardiovascular defects.**
- **Atypical antipsychotics can cause weight gain, gestational diabetes, and metabolic syndrome with poor obstetric outcomes.**

Chronic Illnesses in Pregnancy

6. Thyroid disorders:

- Untreated hypothyroidism increases the risk of preeclampsia, premature birth, miscarriage, growth restriction, and impaired neurological development in the fetus.
- Thyroid replacement should be instituted with 0.1 mg/day levothyroxine.
- Women taking thyroid replacement before pregnancy usually have increased requirement during pregnancy.
- Follow TSH level during pregnancy every 4-6 weeks for dose titration.

Chronic Illnesses in Pregnancy

- **Hyperthyroidism during pregnancy is associated with fetal death, low birth weight, intrauterine growth restriction, and preeclampsia.**
- **Therapy include thionamides (methimazole and PTU).**
- **The risks of uncontrolled hyperthyroidism outweigh the risks of thionamides.**
- **Iodine 131 (I^{131}) is contraindicated because of the risk of damage of fetal thyroid.**

Labor and Delivery

1. Preterm labor:

- Preterm labor occurs between 20-37 weeks of gestation.
- It is a leading cause of infant morbidity and mortality.

Tocolytic therapy:

- The purposes of tocolytic therapy:

1. Postpone delivery to allow for maximal effect of antenatal corticosteroid therapy.

Labor and Delivery

2. **Allow for transportation of the mother to a facility equipped to deal with high-risk deliveries.**
3. **Prolongation of pregnancy when there are underlying, self-limiting conditions that can cause labor (pyelonephritis, abdominal surgery).**

- **Tocolytics are <u>not</u> used beyond 34 weeks of gestation.**

Labor and Delivery

- **Tocolytic therapy should not be used in cases of previability, intrauterine fetal demise, a lethal fetal anomaly, intrauterine infection, fetal distress, severe preeclampsia, vaginal bleeding, or maternal hemodynamic instability.**
- **Tocolytic agents: β-agonists, magnesium, calcium channel blockers, and prostaglandin inhibitors (NSAIDs).**
- **All prolong pregnancy 2-7 days, but do not reduce overall rates of respiratory distress syndrome, neonatal death or preterm delivery.**

Labor and Delivery

β-agonists (terbutaline, ritodrine):

- **Have higher incidence of maternal adverse effects: hypokalemia, arrhythmias, hyperglycemia, hypotension, and pulmonary edema.**
- **Oral dosing or prolonged parenteral (sc) use may be associated with maternal cardiotoxicity and death.**

Labor and Delivery

Intravenous magnesium sulfate:

- **Its use is not supported by evidence of effectiveness as tocolytic agent.**
- **However, it has a neuro-protective role – it decreases the occurance of cerebral palsy.**
- **Maternal adverse effects: pulmonary edema.**
- **Toxic effects: hypotension, muscle paralysis, tetany, cardiac arrest, and respiratory depression.**
- **Dose adjustment is needed in renal dysfunction.**

Labor and Delivery

Nifedipine:

- It is associated with fewer adverse effects than β-agonists and magnesium sulfate.
- One significant adverse reaction is hypotension with consequent effect on uteroplacental blood flow.
- Associated with reduced neonatal morbidity.

Labor and Delivery

NSAIDs (Indomethacin):

- **Associated with increased rate of closure of the ductus arteriosus when used after 32 weeks of gestation, for more than 48 hours.**

Progesterone:

- **Reduce cervical ripening, reduce uterine wall contractility, and modulate inflammation.**
- **It prevents spontaneous preterm birth**

Labor and Delivery

Atenatal Corticosteroids:

- **Used for fetal lung maturation to prevent respiratory distress syndrome, intraventricular hemorrhage and death of infants in premature delivery.**
- **Betamethasone 12 mg/day IM for 2 doses.**
- **Dexamethasone 6mg IM every 12 hours for 4 doses.**

  (between 24-34 weeks of gestation)

Labor and Delivery

Group B *Streptococcus* (GBS) infection:

- **Maternal infection with GBS is associated with invasive disease of the newborn.**
- **Associated with increased risk of pregnancy loss, premature delivery, and transmission of the bacteria to the infant during delivery.**
- **Neonatal infections include bacteremia, pneumonia, meningitis leading to fatality.**
- **Penicillin G 5 million units given IV, followed by 2.5 million units every 4 hours until delivery is the recommended treatment.**

Labor and Delivery

- **Ampicillin is an alternative at 2g IV followed by 1g every 4 hours until delivery.**
- **In women with penicillin allergy but not at risk of anaphylaxis, cefazolin 2g IV, followed by 1g every 8 hours.**
- **In women with high risk of anaphylaxis, clindamycin 900 mg IV every 8 hours, or erythromycin 500 mg IV every 6 hours.**
- **If resistent for clindamycin and erythromycin, vancomycin 1g IV every 12 hours until delivery.**

Labor and Delivery

Cervical Ripening and Labor Induction:

- Cervical ripening is mediated by hormonal changes, including final mediation by prostaglandin E_2 and $F_{2\alpha}$ which increase collagenase activity in the cervix leading to thinning and dilation.
- Concerns with induction of labor are ineffective labor and hyperstimulation that may adversely affect the fetus.

Labor and Delivery

- **Prostaglandin E_2 analogs (dinoprostone) are commonly used for cervical ripening administered intracervically. The patient should remain supine for 30 min.**
- **The insert is removed when labor begins or after 12 hours.**
- **The patient should be attached to the fetal heart monitor for the entire period of insertion and 15 min after its removal.**

Labor and Delivery

- Prostaglandin E_1 analogs (Misoprostol) can be used and is effective.
- More effective when inserted intravaginally.
- Adverse effects: hyperstimulation, and meconium-stained amniotic fluid.
- Misoprostol is containdicated in women with previous uterine scar because of its association with uterine rupture.

Labor and Delivery

- **Oxytocin is most commonly used for labor induction after cervical ripening.**

Labor Analgesia:

1. **The first phase of labor starts from onset of labor to complete cervical dilation. Women perceive visceral pain because of uterine contractions.**
2. **The second phase of labor is the period between complete cervical dilation and delivery. Women perceive visceral pain because of perineal stretching.**

Labor and Delivery

Pharmacologic approach to labor pain management:

1. Parenteral opioids:

- **Commonly used to alleviate labor pain.**
- **In comparison with epidural analgesia, they have lower rates of oxytocin augmentation, result in shorter stages of labor, and require fewer instrumental deliveries and cesarean section for fetal distress.**

Labor and Delivery

2. Epidural analgesia:

- **Better pain relief than other analgesic modalities.**
- **Constitutes administration of an opioid or an anesthetic (fentanyl and/or bupivacaine) into the epideural space.**
- **Combined spinal/epidural anesthesia have a shorter time of onset of analgesia.**

Labor and Delivery

- **Adverse effects: hypotension, pruritus, inability to void, prolongation of the first and second stages of labor, higher numbers of instrumental deliveries and cesarean section for fetal distress, nausea and vomiting, and maternal fever.**
- **Rarely, puncture of subarachnoid space leading to sever headache.**