- Avoided during pregnancy:
  1. Sodium bicarb and magnesium trisilicate. electrolytes imbalance. Castor oil Mineral oil
  2. Metoclopromide and phenothiazines. EPS (dystonia)
  3. Ondansterone (Serotonin 5-HT ant.) — oral clefts
  4. Corticosteroides in the first trimester — oral clefts
  5. Cotrimoxazole

Therapy of Certain Disorders During Pregnancy

Yacoub Irshaid MD, PhD, ABCP

Department of Pharmacology, Faculty of Medicine

Pharmacokinetic Changes During Pregnancy

- Normal physiologic changes that occur during pregnancy may alter medication effects, resulting in the need to monitor or adjust dose or type of 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.

Everything in plasma becomes diluted

they will be eliminated faster

Pharmacokinetic Changes During Pregnancy

- **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 due to dilution, which increases the volume of distribution of highly protein-bound drugs.**
- **Unbound drug is also rapidly eliminated by the liver or the kidney.**

They need higher doses for some drugs like protein-bound ones than those non-pregnant.

↑ free fr of these highly protein bound drugs, and with the ↑ in GFR and ↑ hepatic perfusion; there'll be increased elimination of this drug.

↑ Fluid; ↑ conc. of water soluble drugs.

Pharmacokinetic Changes During Pregnancy

- **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 acid may affect absorption of weak acids and basis.**
- **High levels of estrogen and progesterone may affect hepatic enzyme activity.**

due to ↑ PRG.

As mentioned before, this will delay absorption of drugs from the small intestines.

↑acid → ↑absorption of acidic drugs

Basic won't be absorped

mainly estrogen (inducers of drug metabolism).

Pregnancy-Influenced Issues

- **Pregnancy causes or exacerbates 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.**

↑ pressure of uterus over veins + ↑ constipation

thus they'll need treatment.

Pregnancy-Influenced Issues

1. GIT:

A. 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 softener is appropriate.**

Pregnancy-Influenced Issues

* Supplemental fibers:

use in sequence

- **Bulk-forming agents (psyllium, methylcellulose, and polycarbophil) are safe for long-term use because they are not absorbed.**

  Husks (fluids are needed along with it)

  bc. they're not absorbed

- ***Osmotic laxative (polyethylene glycol, lactulose, and sorbitol) and stimulant laxatives (Senna and bisacodyl) can be used.**

  if fibers failed.

- **Use of magnesium and sodium salts may cause electrolyte imbalance.**

  Should be avoided

Pregnancy-Influenced Issues

- **Castor oil should be avoided because it stimulates uterine contractions, causes diarrhea, dehydration, and GIT adverse effects (abdominal pain, nausea & vomiting).**
- **Mineral oil impairs fat-soluble vitamin (ADEK) absorption, and may cause severe bleeding in the newborn if used for long time.**
- **Hemorrhoides should be treated conservatively.**

Pregnancy-Influenced Issues

more difficult to treat than peptic ulcer.

B. Management of gastro-esophageal reflux disease includes:

use in sequence

- **Life-style and dietary modification** (small frequent meals, avoiding spicy and fatty meals, **alcohol and tobacco avoidance**, **food avoidance at bedtime**, elevation of the head of the bed).
- **If symptoms are not relieved, antacids** (aluminum, **calcium** or magnesium preparations) and **sucralfate** are acceptable.

better than large infrequent

Maalox

rebound acid secretion: acid secretion increase more than it was before the treatment.

surface acting agent (forms a film over the stomach mucosa ∴ "it improves the mucosal barrier against acid"

∴ ↓ pain and irritation due to ↑ acid.

Pregnancy-Influenced Issues

use in sequence

- Sodium bicarbonate (sodium overload) and magnesium trisilicate (no data available on safety) should be avoided.
  - more water retention = more expansion of plasma volume.
  - Category C
- If the patient does not respond, histamine H_2-receptor blockers (ranitidine) can be used.
- Proton pump inhibitors (omeprazole) may not be associated with increased risk of major birth defects.
  - not used except ***
  - Category C

Pregnancy-Influenced Issues

C. **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.** early on and even sometimes before knowing she's pregnant. peeks at 5th month. normally it's not severe but if it was then it's
- ***Hyperemesis gravidarum*** **(severe vomiting causing weight loss, dehydration, electrolyte imbalance, and ketonuria) occurs in 0.5-2% of women.** thus need active treatment, while simple nausea and vomiting are treated firstly with conservative measures.

use in sequence

Pregnancy-Influenced Issues

use in sequence

- **Dietary modifications such as eating frequent small soft meals, and avoiding fatty and spicy meals may be helpful.**
- **Ginger (الزنجبيل) is effective and probably safe.** (used in IBS also; it relaxes the GTT, but if it was overused it might cause constipation.)
- **Pyridoxine (vitamin B_6) and/or antihistamines (doxylamine) are effective and are first-line agents (Pyridoxine - doxylamine).** (*specifically this one)

Pregnancy-Influenced Issues

- **Metoclopramide and phenothiazines may cause sedation and extrapyramidal adverse effects including dystonia.**
- **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.**

→ Antiemetic agents that are usually used in cancer chemox.

Dexamethasone which is a very good antiemetic.

Pregnancy-Influenced Issues

2. Gestational diabetes (GDM):

- GDM is diabetes diagnosed during the second and third trimester. > 20 weeks
- It develops in 3-5% of pregnant women. not necessarily to develop DM in the future.
- Nutritional education with dietary modifications, exercise and blood glucose monitoring are considered first-line for all women with GDM. Insulin is the first

Pregnancy-Influenced Issues

- **85% of patients can achieve control with this first-line therapy.** Diabetic women on oral hypoglycemics should switch to insulin during pregnancy.
- **Human insulin is the drug of choice for GDM because it does not cross the placenta.** Thus the fetus won't be affected (no macrosomia)
- ~~**Glyburide and metformin are alternatives but long-term safety data are limited.**~~
- **Risks of GDM include: fetal loss, increased risk of congenital malformations, and macrosomia.**

Pregnancy-Influenced Issues

3. Hypertensive disorders of pregnancy:

- **Complicate ~ 10% of pregnancies, and Include:**

1) **Gestational hypertension (without proteinuria developing after 20 weeks of gestation).**
2) **Preeclampsia/eclampsia.**
3) **Chronic hypertension (preexisting hypertension or developing before 20 weeks of gestation).**
4) **Chronic hypertension with superimposed preeclampsia.**

Pregnancy-Influenced Issues

We don't want it lower than this to maintain the feto-placental circ.

- Defined as blood pressure > 140/90.
- Non-drug management: stress reduction, and exercise. (aerobic)
- Activity restriction (?): prolonged bed rest may increase the risk of venous thrombo-embolism.
- Use of supplemental calcium 1-2 g per day decreases the risk of hypertension and preeclampsia in patients with initial low calcium intake.

Pregnancy-Influenced Issues

- Calcium supplements are not effective in patients with adequate calcium intake.
- Initial drug choices include methyldopa, hydralazine, or labetelol.
  - First drug of choice despite its many adverse effects.
  - mixed α-β blocker
  - β-blockers are not recommended in pregnancy bc they reduce the cardiac output thus affecting the feto-placental exchange except labetalol bc it's a vasodilator also.
- ~~Oral nifedipine may be used (slow release, not fast-acting).~~
  - it quickly drops the BP and causes Steal syndrome.
- Magnesium sulfate when preeclampsia is present.

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. needs admission.
- May be prevented by low dose aspirin.
- Magnesium sulfate is effective in preventing eclampsia and treating its seizures.
  - This needs high fluid administration that might cause fluid overload and pulmonary edema + HF
- 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.

Teratogenic

- LMWH needs to be monitored through anti activated factor X activity in 3 cases:
1- Pregnancy
2- Obesity.
3-

Pregnancy-Influenced Issues

Heparin

Drug of choice for VTE in pregnancy.

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.

* 45:35

be it's easy to give and doesn't need extensive monitoring.

Can't cross the placenta

- 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 may produce:**
- **Nasal hypoplasia.**
- **Stippled epiphysis (chondodysplasia punctata).**
- **Limb hypoplasia.**
- **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.
- High risk women with prosthetic heart valves may also receive low-dose aspirin of 75-100 mg/day.

not 60-81 as for women at risk of preeclampsia.

Pregnancy-Influenced Issues

- LMWH should be adjusted to achieve a peak anti-Xa level (0.7 - 1.2 U/mL) at 4 hour post-subcutaneous dose.

2 → till distribution ends and elimination phase begins.

- This recommendation may be associated with subtherapeutic trough level.
- 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 U/mL.

Acute Care Issues in Pregnancy

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

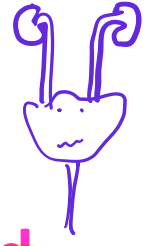
- ***Escherichia coli* is the primary cause of infection in 75-90 % of cases.**
- **Other gram-negative rods (*Proteus* and *Klebsiella*), as well as, group B *Streptococcus* (GBS) may cause UTI.**
- **The presence of GBS in urine indicates heavy colonization of the genitourinary tract, increasing the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

? should be treated and eradicated

if the infection was at the end of pregnancy.

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 [*amoxacillin and *cephalosporins] and *nitrofurantoin.



Not fluoroquinolones as general population

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.

definite pathological dx is needed if E.coli or others ①

1 Nitrofurantoin is not active against *Proteus* species and should not be used after week 37 in ② 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.

contraindicated throughout the pregnancy.

2

1- Highly protein bound ∴ ↑unbound bilirubin → Kernicterus.
2- Folic acid deficiency.

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.**

water soluble → doesn't cross placenta

penicillinase inhibitor.

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.**

bc it's excreted in the urine and diluted in the plasma ∴ conc. is not enough in the renal tissue to treat pyelonephritis.

Nitrofurantoin:
1) For asymptomatic bacteruria
2) Cystitis.
3) Not for proteus.
4) Not for pyelonephritis.

Acute Care Issues in Pregnancy

Treatment for some sexually transmitted diseases in pregnancy:

1. **Bacterial vaginosis:** Anaerobic bacteria.
   Recommended: Metronidazole.
   Alternative: Clindamycin.
2. **Chlamydia:** Macrolide Abs.
   Recommended: Azithromycin.
   Alternative: Erythromycin.

Acute Care Issues in Pregnancy

3. **Genital herpes:**

   Recommended: Acyclovir or valacyclovir.

4. **Gonorrhea:**

   along with probenecid

   Recommended: Ceftriaxone , treat chlamydial infection concurrently.

   Alternative: Azithromycin.

5. **Trichomoniasis:**

   Recommended: Metronidazole

   Tinidazole should be avoided during pregnancy.

Chronic Illnesses in Pregnancy

1. Allergic Rhinitis:

- **Treatment strategies for allergic rhinitis in pregnancy are similar to non-pregnant women: avoidance of allergen, immunotherapy, and pharmacotherapy.**
- **Drugs that can be used: intranasal corticosteroids, intranasal cromolyn, and first-generation antihistamines (chlorpheniramine, diphenhydramine, and hydroxyzine.**
- **Topical oxymetazoline (α-agonist) may be preferable to oral decongestants.**

Chronic Illnesses in Pregnancy

2. **Bronchial 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.**

Chronic Illnesses in Pregnancy

Treatment:

1. **Step 1: short-acting β_2-agonists (SABA), albuterol + inhalational corticosteroids, budesonide.**
   = salbutamol
2. **Step 2: long-acting β_2-agonists (LABA), [redacted] + inhalational corticosteroids, budesonide.**
   → after treating the acute attack through step 1.
   salmetrol

Chronic Illnesses in Pregnancy

3. **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 glyburide and metformin.**~~

Chronic Illnesses in Pregnancy

3. **Epilepsy:**

- **Seizure frequency does not change for most pregnant women with epilepsy.**
- **Seizures may become more frequent because of changes in:**

a) **maternal hormones.**

b) **sleep deprivation.**

c) **medication adherence problems because of fear of teratogenic risk.**

Chronic Illnesses in Pregnancy

d) changes of free serum concentration of antiepileptic drugs resulting from:

i. increased maternal volume of distribution.

ii. decreased protein binding from hypoalbuminemia. due to dilution ↑ drug free fraction. + ↑ elimination.

iii. increased hepatic drug metabolism. due to ↑ perfusion

iv. increased renal drug clearance. ↑ GFR due to ↑ plasma volume

Chronic Illnesses in Pregnancy

So pregnant ladies should be kept treated → preferably with a single drug

- **The risks of uncontrolled seizures to the infant are greater than those associated with antiseizure drugs.** (Teratogenicity) **(especially for tonic-clonic seizures).** (but)
- **Major malformations are 2-3 times more likely to occur in children born to women taking antiseizure drugs than to those who do not.**

Chronic Illnesses in Pregnancy

But which antiepileptic should be used?

ASDs status:

a. **Probably safest AEDs**: **Carbamazepine, lamotrigine, levetiracetam, ~~phenytoin~~ (??).**

b. **Lower risk than valproic acid (VPA): Gabapentin, oxcarbazepine, zonisamide.**

c. **Significant risk: VPA, topiramate, phenobarbital.**

~> regarding teratogenicity

valproic acid (worse teratogenic)

→ Should not be used.

bc: (long $t_{1/2}$ = 4 days + very sedative agent)

used for: { febrile seizures / neonatal seizures

Chronic Illnesses in Pregnancy

- Use of valproic acids should be avoided during 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.
- Antiseizure drug monotherapy is recommended with dose optimized before conception.

1
2
3
~ physiological not anatomical. like mental retardation.

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 !!

Risk of Antiseizure Drugs During Pregnancy

https://obgyn.onlinelibrary.wiley.com/doi/pdf/10.1111/tog.12413

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4784252/pdf/10.1177_1756285615623934.pdf

When to avoid or postpone pregnancy?

1. **Uncontrolled epilepsy**
2. **Drug-resistant epilepsy**
3. **Polytherapy**
4. **High dose ASDs** meaning she has drug response problem
5. **Non-compliance**
6. **Poor general health**

Chronic Illnesses in Pregnancy

4. Chronic hypertension of pregnancy:

Defined as :

1) hypertension occurring before 20 weeks of gestation
2) the use of antihypertensive medications before pregnancy
3) or the persistence of hypertension beyond 12 weeks postpartum.

Classified as:

a. Mild/non-severe: 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 you should be careful NOT to compromise utero-placental blood flow. (Lower BP over a period of hours). → so adaptation occurs.
- If there is no end organ damage, antihypertensive drugs may not be used 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. 140/90

Drugs:

- Initial choice include methyldopa, hydralazine, or labetelol.
- ~~Oral slow-release nifedipine may be used, but not fast-acting nifedipine.~~
- Magnesium sulfate when preeclampsia is present.

Chronic Illnesses in Pregnancy

- ACEis, ARBs, renin inhibitors (aliskiren), and mineralocorticoid receptor antagonists should be avoided, because of teratogenicity and toxicity to fetus.
- Atenolol may be associated with fetal growth restrictions.
- Thiazides ~~are second line.~~ They reduce plasma volume.

Therapy of Hypertension

Treatment of Chronic Hypertension in Pregnancy

Drug/Class	Comments
Methyldopa	Long-term follow-up data supports safety; considered a preferred agent
Labetalol	Increasingly used over methyldopa because of fewer side effects; considered a first-line agent
ACEi, ARB, direct renin inhibitor	Contraindicated; major teratogenicity reported with exposure (fetal toxicity and death)
β-Blockers	Intrauterine growth retardation reported (mostly with atenolol)
Clonidine, thiazides, CCBs	Limited data

nifedipine

Chronic Illnesses in Pregnancy

6. **Thyroid disorders:**

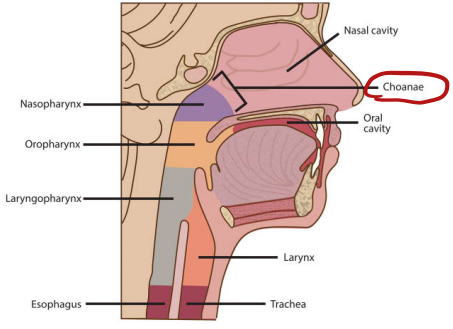
- **Untreated hypothyroidism increases the risk of preeclampsia, premature birth, miscarriage, growth restriction, and impaired neurological development in the fetus.**
- **Thyroid replacement should be instituted with 0.1 mg/day levothyroxine.**

Chronic Illnesses in Pregnancy

- Women taking thyroid replacement before pregnancy usually have increased requirement during pregnancy.
- Follow TSH level during pregnancy every 4-6 weeks for dose titration.
- Hyperthyroidism during pregnancy is associated with fetal death, low birth weight, intrauterine growth restriction, and preeclampsia.

Chronic Illnesses in Pregnancy

- **Therapy include thionamides (methimazole and propylthiouracil (PTU).**
- **Use PTU in first trimester (it is significantly ionized at physiologic pH), and switch to methimazole in second & third trimesters to balance the risk of PTU-induced hepatotoxicity, and methimazole embryopathy (Choanal and esophageal atresia).**



Chronic Illnesses in Pregnancy

- **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.**

radioactive

and this causes mental retardation

Labor and Delivery

1. Preterm labor:

Age of viability

- 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:

Delay labor

1. Postpone delivery to allow for maximal effect of antenatal corticosteroid therapy. ~that was given by you when you suspected premature labor. (to prevent ARDS and aid in surfactant maturation).

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 not 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.

selective β2 to relax the uterus, and not stimulate the heart.

Labor and Delivery

selectivity + dose are important to each other.

β_2-agonists (terbutaline, ritodrine):

- **Have higher incidence of maternal adverse effects: hypokalemia, arrhythmias, hyperglycemia, hypotension, and pulmonary edema.**

extracellular → intracellular shift

at higher doses, those drugs lose selectivity.

β2 receptors in MSS → vasodilation

left sided HF.

- **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 neuroprotective role – it decreases the occurrence 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.

occurs due to brain hypoxia during delivery and MgSO4 stabilizes vasculature and protects the brain from damage

bc we mentioned, alot of fluids are required...

Labor and Delivery

Nifedipine (slow release):

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

Labor and Delivery

don't start with it.
- 50% increase of blood volume within few days
- cardiotoxic

NSAIDs (Indomethacin):

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

Normally we use tocolytics for 2-7 days.

Progesterone:

- Reduces cervical ripening, reduces uterine wall contractility, and modulates inflammation.
- It prevents spontaneous preterm birth

imp

Labor and Delivery

Antenatal Corticosteroids:

- Used for fetal lung maturation to prevent respiratory distress syndrome, intraventricular hemorrhage and death of infants in premature delivery. (given to the mother)
- Betamethasone ~~12 mg/day IM for 2 doses.~~
- Dexamethasone ~~6 mg 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 resistant of clindamycin and erythromycin, vancomycin 1g IV every 12 hours until delivery.

Labor and Delivery

Cervical Ripening and Labor Induction:

dilation and effacement of cervix

- 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.

∴ fetal distress

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. even if labor didn't occur.
- 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 analog, Misoprostol, can be used and is effective.
  Adverse effect: diarrhea
  used to treat NSAIDS induced peptic ulcers, but later on PPIs were found to be more effective.
- More effective when inserted intravaginally.
- Adverse effects: hyperstimulation of uterus, and meconium-stained amniotic fluid.
- It is containdicated in women with previous uterine scar because of its association with uterine rupture.
- Oxytocin is most commonly used for labor induction after cervical ripening.
  small dose IV infusion
  may be associated with hyperstimulation.

Labor and Delivery

• Different perception.

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:**

- **May be used to alleviate labor pain.**
- **Maternal adverse reactions: drowsiness, nausea, vomiting.**

fetal withdrawal syndrome

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 epidural space.**

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 than opioid analgesia, nausea and vomiting, and maternal fever.
- Rarely, puncture of subarachnoid space leading to sever headache.

Labor and Delivery

Analgesic rather than anesthetic (not hypnotic).

3. **Nitrous oxide (laughing gas):**

- **It is an inhaled anesthetic gas that may help reduce anxiety and make patients less aware of pain, but does not eliminate it.**

it improves the perception of pain by the pt.

- **Many patients ask for another method of analgesia, epidural analgesia.**
- **Nitrous oxide was found to be safe for the newborns.**