TABLE OF CONTENTS

Anticoagulation considerations in the pregnant patient
- Overview
- Treatment Options
  - UFH
  - LMWH
  - Warfarin

Cervical Ripening Agents – comparison chart

Common OB/GYN/Neonatal Abbreviations

Drugs in Pregnancy and Lactation (powerpoint)
- Congenital malformations
- Drug transfer properties in human milk
- Drugs contraindicated in breastfeeding mothers
- Drugs contraindicated in pregnancy
- FDA drug risk classification
- Guidelines for selecting drugs in nursing mothers
- Human Teratogenesis
- Lactation drug risk categories
- Physiologic changes affecting pharmacokinetics during pregnancy
- Physiology of lactation
- Placental drug transfer properties
- Principles of drug use in pregnancy
- Teratogen Information Service

MSCU emergency drug box – exchange procedure and medication contents and dosing

OB-GYN pearls: (powerpoint)
- Anticoagulation in the pregnant patient
- Chorioamnionitis
- Common medications:
  - Pitocin
  - Methotrexate (MTX)
  - Misoprostol
  - Prostaglandin gels
- Gestational Diabetes – White’s classification
- Handling of transfer orders
- HELLP syndrome
- Hutzel Hospital Nursing Unit Description
- Maternal Testing
  - Glucose Challenge Test
  - Group B Streptococcus (GBS)
  - Maternal testing – serum markers
  - Tests of fetal lung maturity
  - First trimester testing (Hepatitis B surface antigen, HIV, RPR, Rubella, Gonorrhea, Chlamydia, Blood type)
- Medication Emergency Box in MSCU
- Pharmacokinetics in the pregnant patient
- PIH
- Placental drug transfer properties
- Post partum endometritis
- Preterm labor (PTL)
- Rh Incompatibility
- Treatment of VTE
- Vancomycin for GBS prophylaxis and CMD criteria

Pharmacokinetic review of antibiotics in OB/GYN population

Zidovudine – stat orders for the pregnant patient in active labor
Pregnancy alone increases the risk of venous thrombosis five-fold and is the leading cause for maternal deaths. The hypercoagulable state of pregnancy accounts for this increased risk and is related to increases in clotting factors, increase in venous stasis, decreases in natural inhibitors of coagulation and complications from the delivery itself such as placental abruption, infection and cesarean sections.

Anticoagulation of the pregnant patient is required for:
1) Treatment of acute events
2) Prophylaxis of patients with a history of a thrombotic event.
3) Valvular heart disease
4) Acquired Antiphospholipid syndrome
5) Inherited Factor V Leiden, Protein C, Protein S, Antithrombin III, Prothrombin 20210 mutation.
6) Short course Heparin treatment for post-partum treatment of septic pelvic thrombosis.

Treatment options

Heparin
UFH and LMWH are the anticoagulants of choice in the pregnant patient since it does NOT cross the placenta. UFH is classified a pregnancy category C. There is a reduced bioavailability of heparin during pregnancy secondary to:
1) Increase in heparin binding proteins
2) Increase in plasma volume
3) Increase in renal clearance
4) Heparin degradation by the placenta
It is also difficult to maintain a therapeutic APTT through entire dosing interval.

Dosing:
Prophylaxis:
Initial: Heparin 5000 Units SC q12
This dose is NOT adequate in the 2nd and 3rd trimester.
May need 7500 – 10000 Units SC q12

Treatment for DVT/ PE:
IV heparin
80U/kg Heparin loading dose (Use TBW unless 30% over IBW then use ABW)
18U/kg/hr Heparin continuous infusion (Use TBW unless 30% over IBW then USE Adjusted Body Weight)
Target APTT 48-78 seconds (1.5-2.5 control)
Follow DMC nomogram for adjustments but keep in mind that small changes in rate or bolus doses can markedly increase or decrease APTT levels. Max initial loading dose of 10000 units and maximum initial continuous infusion 2300U/hr.

**Heparin for valvular heart disease:** Target APTT 2-2.5 times control (APTT target must be maintained throughout dosing interval for subcutaneous dosing).

**Treatment course for Septic Pelvic Thrombosis (SPT)** is short and generally <5 days for IV heparin along with broad spectrum antibiotics (Ampicillin, Gentamicin, Clindamycin/Metronidazole)

**IV to SQ dosing**
1) Calculate 24 hour heparin infused.
2) Multiply by a factor of 1.2
3) Divide by 2 for q12 dosing or by 3 for q8 dosing.
4) Round dose to even number. Volume of dose should not exceed 2ml and needle used is 25 guage 5/8 inch needle or 1 inch needle for obese patients.
5) APTT levels drawn 6 hours post doses for each level checked.

**SQ to IV dosing**
1) Calculate 24 hour heparin injected.
2) Multiply by a factor of 0.8
3) Round dose to even number.

**Side Effects:**
1) Heparin induced thrombocytopenia (3%)
2) Heparin induced osteoporosis
3) Hemorrhage

**Compatibility with breastfeeding:**
Heparin is considered compatible with breastfeeding due to poor oral bioavailability and large molecular weight of heparin that would not pass into breast milk to clinically significant levels.

**Coumadin**
The use of Warfarin in this patient population is controversial but has been reported. Coumarrin derivatives **DO** cross the placenta. They have the potential for fetal bleeding and causing teratogenicity. This drug is classified as Category D but does potentially have a limited role in anticoagulation in the pregnant patient. This is generally reserved for patients with valvular disease who have failed treatment with Heparin or Low Molecular Weight Heparins (LMWH).

**Treatment:**
1) **AVOID** Warfarin from 6-12th weeks gestation
2) Continue Warfarin from 13th week up to 34-36 weeks gestation.
3) Patient is then switched to Heparin or LMWH until delivery, which is generally a scheduled induction.
Side Effects:
Embryopathy (stippled epiphyses, nasal and limb hypoplasia), bleeding
CNS abnormalities (dorsal midline hypoplasia), fetal loss 8-50%

Compatibility with breastfeeding:
Warfarin is considered compatible with breastfeeding by the AAP.
(highly protein bound)

LOW MOLECULAR WEIGHT HEPARIN (LMWH)
Low molecular weight heparins do not cross into fetal circulation. LMWH
and UFH are the anticoagulants of choice in the pregnant patient. They do not
bind to numerous plasma proteins and as a result do not have a saturation
kinetics phase of elimination. Bioavailability is also greater and unchanged at
different doses. Pregnancy Category B but data is limited and largely European.
LMWH have potential advantages over UFH during pregnancy:
1) Less HIT (Heparin Induced Thrombocytopenia)
2) Longer Plasma half-life
3) More predictable dose response than UFH

Dosing:
Prophylaxis dose:
Enoxaprin (Lovenox®) 30mg SC BID
1) There are reports of decreased clearance using prophylactic doses of
enoxaparin in the 3rd trimester (after 32 weeks)
2) BID dosing is recommended over QD dosing since the half-life of LMWH
is decreased in pregnancy.
3) Target aXa levels (0.2-0.6 Unit/mL)

Treatment dose:
Enoxaparin 1mg/kg/dose SC q12 (Use Adjusted body weight if 30% above
BW or use TBW of early pregnancy).
Maximum initial dose 150mg SC BID
1) Monitor aXa levels (Target therapeutic range: 0.5-1.2 Unit/mL)

Side effects:
1) Decreased risk of osteoporosis compared to UFH
2) Hemorrhage

Compatibility with breast feeding
Considered compatible due to poor oral bioavailability and large molecular
weight that is too large to produce clinically relevant levels in human milk.
**Treatment options for the Pregnant patient with Prosthetic Heart Valves:**

1) Adjusted dose BID LMWH throughout pregnancy. Keep target aXa level 1-2 Unit/mL
2) Aggressive adjusted dose UFH throughout pregnancy SC q12 to keep mid-interval PTT 2x control (or anti-Xa heparin level of 0.35 to 0.7 Unit/ml)
3) UFH or LMWH until the 13th week gestational age then switch to Warfarin until the middle of the third trimester and then restart UFH or LMWH.
4) Patients at a high risk with prosthetic heart valves should also consider use of low-dose aspirin (up to 160mg/day).

**Direct Thrombin inhibitors**

Direct Thrombin inhibitors such as Hirudin cross the placenta and have yet to be evaluated during pregnancy.
<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>INTERVAL</th>
<th>MAX DOSE</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>CONTRAINDICATIONS</th>
<th>COST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxytocin (Pitocin®)</td>
<td>1-6 mU/min</td>
<td>IV</td>
<td>Increase dose in increments of 15-60min</td>
<td>25mU/min</td>
<td>-short half-life -potent and easy to titrate -dose related side effects -does not cross placental barrier -generally well tolerated -can be used for VBAC deliveries</td>
<td>-anti-diuretic effect at high doses -uterine hyperstimulation -uterine rupture</td>
<td>VBAC deliveries??? -fetal distress -cephalopelvic disproportion -unfavorable fetal position -hyperactive uterus</td>
<td>Med: 0.39cents + IV + nursing time + pump Roughly estimated as $50-100</td>
</tr>
<tr>
<td>Prostaglandin gels (compounded from Dinoprostone 20mg Supp)</td>
<td>2mg/5ml</td>
<td>Intravaginal</td>
<td>Q6hr</td>
<td>3gels/24hr</td>
<td>-cost compared to commercially available Prepidil® and Cervidil®</td>
<td>-compounded by pharmacy -must be refrigerated</td>
<td>VBAC deliveries??? -cephalopelvic disproportion -hyperactive uterus -multipara &gt;=6 -placental previa -vaginal bleeding -Vaginal delivery not indicated ex: HSV</td>
<td>$40</td>
</tr>
<tr>
<td>Misoprostol (Cytotec®)</td>
<td>25-50mcg</td>
<td>Intravaginal</td>
<td>Q4-6hr</td>
<td>6-8dose</td>
<td>-cost -convenience -no refrigeration required</td>
<td>-tachysystole -uterine hyperstimulation -higher incidence of meconium staining -uterine rupture -bioavailability of vag administration is 3x greater than oral administration</td>
<td>-VBAC deliveries -Previous infections -Hyperactive uterus</td>
<td>0.44 cents/0.1mg tab</td>
</tr>
<tr>
<td>Dinoprostone insert (Cervidil®)</td>
<td>10mg</td>
<td>Intravaginal</td>
<td>Vag insert x1 dose</td>
<td>One</td>
<td>-one time dose -constant release of medication @ 0.3mg/hr -inserted and removed more easily if uterine hyperstimulation occurs</td>
<td>-cost -uterine hyperstimulation -uterine rupture</td>
<td>VBAC deliveries??? -fetal distress -multipara &gt;=6 -simultaneous IV oxytocin -vaginal bleeding -cephalopelvic disproportion</td>
<td>$175/insert</td>
</tr>
<tr>
<td>Dinoprostone gel (Prepidil®)</td>
<td>0.5mg gel</td>
<td>Intracervical</td>
<td>Q6hr</td>
<td>3gels/24hr</td>
<td>-commercially available gel -gels must be kept refrigerated -uterine hyperstimulation -uterine rupture</td>
<td>-cost -uterine hyperstimulation -uterine rupture</td>
<td>VBAC deliveries??? -cephalopelvic disproportion -hyperactive uterus -multipara &gt;=6 -placental previa -vaginal bleeding -Vaginal delivery not indicated ex: HSV</td>
<td>$125/gel</td>
</tr>
</tbody>
</table>

Contraindications to cervical ripening:
- Uterine scars
- Uterine anomalies
- Prior molar pregnancy
- Hx of Placenta Percreta
- Hx of Placenta Previa
- Difficult forceps delivery
- Malpresentation
- Fetal anomaly
- Obstructed labor
- Induction of labor
- Uterine hyperstimulation
- Fetal distress
- Vaginal Bleeding
- VBAC???
- Vaginal delivery not indicated ex: HSV
- PID
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/B</td>
<td>Apnea/Bradycardia</td>
</tr>
<tr>
<td>AB</td>
<td>Abortion</td>
</tr>
<tr>
<td>ABO</td>
<td>Blood types A, B and O</td>
</tr>
<tr>
<td>AF</td>
<td>Amniotic fluid</td>
</tr>
<tr>
<td>AFP</td>
<td>Alpha-fetoprotein</td>
</tr>
<tr>
<td>AFV</td>
<td>Amniotic fluid volume</td>
</tr>
<tr>
<td>AGA</td>
<td>Appropriate for gestational age</td>
</tr>
<tr>
<td>Amnio</td>
<td>Amniocentesis</td>
</tr>
<tr>
<td>ANA</td>
<td>Antinuclear antibody</td>
</tr>
<tr>
<td>AP</td>
<td>Ante-partum</td>
</tr>
<tr>
<td>APS</td>
<td>Anti-phospholipid syndrome</td>
</tr>
<tr>
<td>AROM</td>
<td>Artificial rupture of membranes</td>
</tr>
<tr>
<td>ASD</td>
<td>Atrial septal defect</td>
</tr>
<tr>
<td>BBT</td>
<td>Basal body temperature</td>
</tr>
<tr>
<td>BCP</td>
<td>Birth Control Pill</td>
</tr>
<tr>
<td>BHCG</td>
<td>Beta human chorionic gonadotropin</td>
</tr>
<tr>
<td>BM</td>
<td>Breast milk</td>
</tr>
<tr>
<td>BMZ</td>
<td>Betamethasone</td>
</tr>
<tr>
<td>BPD</td>
<td>Bronchopulmonary dysplasia</td>
</tr>
<tr>
<td>BPM</td>
<td>Beats per minute</td>
</tr>
<tr>
<td>BSO</td>
<td>Bilateral Salpingo-oophorectomy</td>
</tr>
<tr>
<td>BTL</td>
<td>Bilateral tubal ligation</td>
</tr>
<tr>
<td>BV</td>
<td>Bacterial vaginosis</td>
</tr>
<tr>
<td>CAH</td>
<td>Congenital adrenal hyperplasia</td>
</tr>
<tr>
<td>CD</td>
<td>Cesarean delivery</td>
</tr>
<tr>
<td>CHORIO</td>
<td>Chorioamnionitis</td>
</tr>
<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td>COA</td>
<td>Coarctation of aorta</td>
</tr>
<tr>
<td>Coomb’s</td>
<td>Direct antiglobulin test</td>
</tr>
<tr>
<td>C-SECT or C/S</td>
<td>Cesarean section</td>
</tr>
<tr>
<td>CST</td>
<td>Contraction stress test</td>
</tr>
<tr>
<td>CVS</td>
<td>Chorionic villus sampling</td>
</tr>
<tr>
<td>Cx</td>
<td>Cervix</td>
</tr>
<tr>
<td>D&amp;C</td>
<td>Dilatation &amp; Curettage</td>
</tr>
<tr>
<td>D&amp;E</td>
<td>Dilatation &amp; Evacuation</td>
</tr>
<tr>
<td>DFA</td>
<td>Direct fluorescent antibody</td>
</tr>
<tr>
<td>DHT</td>
<td>Dihydrotestosterone</td>
</tr>
<tr>
<td>ECMO</td>
<td>Extracorporeal membrane oxygenation</td>
</tr>
<tr>
<td>ECS</td>
<td>Endocervical scrape</td>
</tr>
<tr>
<td>EFW</td>
<td>Estimated fetal weight</td>
</tr>
<tr>
<td>ELBW</td>
<td>Extremely low birth weight</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>EmBx</td>
<td>Endometrial biopsy</td>
</tr>
<tr>
<td>ENNS</td>
<td>Early Neonatal neurobehavioral score</td>
</tr>
<tr>
<td>Epis Med.</td>
<td>Medial episiotomy</td>
</tr>
<tr>
<td>Epis LML</td>
<td>Left mediolateral episiotomy</td>
</tr>
<tr>
<td>Epis RML</td>
<td>Right mediolateral episiotomy</td>
</tr>
<tr>
<td>Epis.</td>
<td>Episiotomy</td>
</tr>
<tr>
<td>FAS</td>
<td>Fetal alcohol syndrome</td>
</tr>
<tr>
<td>FBS</td>
<td>Fasting Blood Sugar</td>
</tr>
<tr>
<td>FBS</td>
<td>Fetal breathe sounds</td>
</tr>
<tr>
<td>FHR</td>
<td>Fetal heart rate</td>
</tr>
<tr>
<td>FHR-UC</td>
<td>Fetal heart rate- uterine contraction</td>
</tr>
<tr>
<td>FHT</td>
<td>Fetal heart tones</td>
</tr>
<tr>
<td>FT</td>
<td>Fetal tone</td>
</tr>
<tr>
<td>FT</td>
<td>Full term</td>
</tr>
<tr>
<td>FTA-ABS</td>
<td>Fluorescent treponemal antibody absorbed</td>
</tr>
<tr>
<td>FTD</td>
<td>Failure to descend</td>
</tr>
<tr>
<td>FTND</td>
<td>Full term normal delivery</td>
</tr>
<tr>
<td>FTP</td>
<td>Failure to progress</td>
</tr>
<tr>
<td>FTT</td>
<td>Failure to thrive</td>
</tr>
<tr>
<td>FUB</td>
<td>Functional uterine bleeding</td>
</tr>
<tr>
<td>FUO</td>
<td>Fever of unknown origin</td>
</tr>
<tr>
<td>G_P_ _ _ _</td>
<td>Gravida (# pregnancies) Para (Prior pregnancies-Term, Preterm, Abortions, Alive)</td>
</tr>
<tr>
<td>GA</td>
<td>Gestational age</td>
</tr>
<tr>
<td>GBS</td>
<td>Group B Streptococcus</td>
</tr>
<tr>
<td>GC or G/C</td>
<td>Gonorrhea/Chlamydia</td>
</tr>
<tr>
<td>GCT</td>
<td>Glucose Challenge Test</td>
</tr>
<tr>
<td>GDM</td>
<td>Gestational diabetes mellitus</td>
</tr>
<tr>
<td>GODM</td>
<td>Gestational onset diabetes mellitus</td>
</tr>
<tr>
<td>GTT</td>
<td>Glucose Tolerance Test</td>
</tr>
<tr>
<td>GU</td>
<td>Genitourinary</td>
</tr>
<tr>
<td>HAV</td>
<td>Hepatitis A Virus</td>
</tr>
<tr>
<td>HBIG</td>
<td>Hepatitis B Immune Globulin</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Hepatitis B surface antigen</td>
</tr>
<tr>
<td>HBV</td>
<td>Hepatitis B virus</td>
</tr>
<tr>
<td>HCG</td>
<td>Human chorionic gonadotropin</td>
</tr>
<tr>
<td>HCV</td>
<td>Hepatitis C virus</td>
</tr>
<tr>
<td>HELLP</td>
<td>Hemolysis, elevated liver enzymes, low platelets</td>
</tr>
<tr>
<td>HIE</td>
<td>Hypoxemic ischemic encephalopathy</td>
</tr>
<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>HLHS</td>
<td>Hypoplastic left heart syndrome</td>
</tr>
<tr>
<td>HMD</td>
<td>Hyaline Membrane disease</td>
</tr>
<tr>
<td>HPV</td>
<td>Human papillomavirus</td>
</tr>
<tr>
<td>HSV</td>
<td>Herpes Simplex Virus</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Definition</td>
</tr>
<tr>
<td>--------------</td>
<td>------------</td>
</tr>
<tr>
<td>HTLV-1</td>
<td>Human T-cell lymphotrophic virus type I</td>
</tr>
<tr>
<td>IDDM</td>
<td>Infant of a drug dependent mother</td>
</tr>
<tr>
<td>Inc AB</td>
<td>Incomplete abortion</td>
</tr>
<tr>
<td>IUCP</td>
<td>Intrauterine contraceptive device</td>
</tr>
<tr>
<td>IUD</td>
<td>Intrauterine device</td>
</tr>
<tr>
<td>IUFD</td>
<td>Intrauterine fetal demise</td>
</tr>
<tr>
<td>IUGR</td>
<td>Intrauterine growth retardation (restriction)</td>
</tr>
<tr>
<td>IUP</td>
<td>Intrauterine pregnancy</td>
</tr>
<tr>
<td>IUPF</td>
<td>Intrauterine pregnancy</td>
</tr>
<tr>
<td>IUTP</td>
<td>Intrauterine term pregnancy</td>
</tr>
<tr>
<td>IVH</td>
<td>Intraventricular hemorrhage</td>
</tr>
<tr>
<td>K-B</td>
<td>Kleihauer-Betcke</td>
</tr>
<tr>
<td>KOH</td>
<td>Potassium Hydroxide</td>
</tr>
<tr>
<td>L/S</td>
<td>Lecithin-to-sphinphomyelin ratio</td>
</tr>
<tr>
<td>LAVH</td>
<td>Laparoscopic assisted vaginal hysterectomy</td>
</tr>
<tr>
<td>LBW</td>
<td>Low birth weight</td>
</tr>
<tr>
<td>LGA</td>
<td>Large for gestational age</td>
</tr>
<tr>
<td>LMP</td>
<td>Last menstrual period</td>
</tr>
<tr>
<td>LSCS</td>
<td>Lower segment c-section</td>
</tr>
<tr>
<td>LSO</td>
<td>Left Salpingo-oophorectomy</td>
</tr>
<tr>
<td>LTCS</td>
<td>Lower transverse Cesarean section</td>
</tr>
<tr>
<td>Mec</td>
<td>Meconium</td>
</tr>
<tr>
<td>MMR</td>
<td>Measles, mumps, rubella</td>
</tr>
<tr>
<td>MPC</td>
<td>Mucopurulent cervicitis</td>
</tr>
<tr>
<td>NB</td>
<td>Newborn</td>
</tr>
<tr>
<td>NBS</td>
<td>New Ballard Score</td>
</tr>
<tr>
<td>NEC</td>
<td>Necrotizing enterocolitis</td>
</tr>
<tr>
<td>NGU</td>
<td>Nongonococcal urethritis</td>
</tr>
<tr>
<td>NRFHT</td>
<td>Non-reassuring fetal heart tones</td>
</tr>
<tr>
<td>NST</td>
<td>Non stress test</td>
</tr>
<tr>
<td>NSVD</td>
<td>Normal Spontaneous vaginal delivery</td>
</tr>
<tr>
<td>NTD</td>
<td>Neural tube defect</td>
</tr>
<tr>
<td>OCP</td>
<td>Oral contraceptive pill</td>
</tr>
<tr>
<td>OCT</td>
<td>Oxytocin Challenge Test</td>
</tr>
<tr>
<td>PAP</td>
<td>Papanicolaou smear</td>
</tr>
<tr>
<td>PAT</td>
<td>Pregnancy at term</td>
</tr>
<tr>
<td>PDA</td>
<td>Patent ductus arteriosus</td>
</tr>
<tr>
<td>PGE1</td>
<td>Alprostadil</td>
</tr>
<tr>
<td>PHH</td>
<td>Posthemorrhagic hydrocephalus</td>
</tr>
<tr>
<td>PID</td>
<td>Pelvic inflammatory disease</td>
</tr>
<tr>
<td>PIE</td>
<td>Pulmonary interstitial emphysema</td>
</tr>
<tr>
<td>PIH</td>
<td>Pregnancy induced hypertension</td>
</tr>
<tr>
<td>PKU</td>
<td>Phenylketouria</td>
</tr>
<tr>
<td>PMP</td>
<td>Previous menstrual period</td>
</tr>
<tr>
<td>PMS</td>
<td>Premenstrual syndrome</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>PNC</td>
<td>Prenatal care</td>
</tr>
<tr>
<td>PNV</td>
<td>Prenatal vitamin</td>
</tr>
<tr>
<td>PObHx</td>
<td>Past obstetrical history</td>
</tr>
<tr>
<td>PPHN</td>
<td>Persistent pulmonary hypertension of newborn</td>
</tr>
<tr>
<td>PPROM</td>
<td>Preterm premature rupture of membranes</td>
</tr>
<tr>
<td>PPTL</td>
<td>Post partum tubal ligation</td>
</tr>
<tr>
<td>PTL</td>
<td>Preterm labor</td>
</tr>
<tr>
<td>PVL</td>
<td>Periventricular leukomalacia</td>
</tr>
<tr>
<td>RDS</td>
<td>Respiratory Distress Syndrome</td>
</tr>
<tr>
<td>Rh</td>
<td>Rhesus blood factor</td>
</tr>
<tr>
<td>ROP</td>
<td>Retinopathy of prematurity</td>
</tr>
<tr>
<td>RPR</td>
<td>Rapid plasma reagent</td>
</tr>
<tr>
<td>RSV</td>
<td>Respiratory Syncytial virus</td>
</tr>
<tr>
<td>RVH</td>
<td>Right ventricular hypertrophy</td>
</tr>
<tr>
<td>SAB</td>
<td>Spontaneous abortion</td>
</tr>
<tr>
<td>SGA</td>
<td>Small for gestational age</td>
</tr>
<tr>
<td>SIDS</td>
<td>Sudden infant death syndrome</td>
</tr>
<tr>
<td>SPT</td>
<td>Septic Pelvic Thrombosis</td>
</tr>
<tr>
<td>SROM</td>
<td>Spontaneous rupture of membranes</td>
</tr>
<tr>
<td>STD</td>
<td>Sexually transmitted disease</td>
</tr>
<tr>
<td>SVD</td>
<td>Spontaneous vaginal delivery</td>
</tr>
<tr>
<td>TAB</td>
<td>Therapeutic Abortion</td>
</tr>
<tr>
<td>TAH</td>
<td>Total abdominal hysterectomy</td>
</tr>
<tr>
<td>TBLC</td>
<td>Term birth living child</td>
</tr>
<tr>
<td>TCA</td>
<td>Trichloroacetic acid</td>
</tr>
<tr>
<td>TDx FLM</td>
<td>Tdx fetal lung maturity</td>
</tr>
<tr>
<td>THAM</td>
<td>Tromethamine</td>
</tr>
<tr>
<td>TOA</td>
<td>Tubo-ovarian abscess</td>
</tr>
<tr>
<td>TOF</td>
<td>Tetrology of Fallot</td>
</tr>
<tr>
<td>TORCH</td>
<td>Toxoplasmosis, Other (Syphilis Hep B, coxsackie virus, Epstein-Barr, varicella-zoster, human parvovirus, Rubella, Cytomegalovirus, Herpes Simplex</td>
</tr>
<tr>
<td>TTN</td>
<td>Transient tachypnea of newborn</td>
</tr>
<tr>
<td>TVH</td>
<td>Total vaginal hysterectomy</td>
</tr>
<tr>
<td>UAC</td>
<td>Umbilical artery catheter</td>
</tr>
<tr>
<td>UC</td>
<td>Uterine contractions</td>
</tr>
<tr>
<td>US</td>
<td>Ultrasound</td>
</tr>
<tr>
<td>UVC</td>
<td>Umbilical venous catheter</td>
</tr>
<tr>
<td>VBAC</td>
<td>Vaginal birth after cesarean section</td>
</tr>
<tr>
<td>VI</td>
<td>Vaginal irritation</td>
</tr>
<tr>
<td>VIP</td>
<td>Voluntary interruption of pregnancy</td>
</tr>
<tr>
<td>VSD</td>
<td>Ventricular septal defect</td>
</tr>
<tr>
<td>VTX</td>
<td>Vertex</td>
</tr>
<tr>
<td>Vx</td>
<td>Vertex presentation</td>
</tr>
<tr>
<td>ZDV</td>
<td>Zidovudine</td>
</tr>
</tbody>
</table>

Prepared by Mirjana Lulic-Botica RPh, Neonatal Clinical Specialist 3/04
Drugs in Pregnancy and Lactation

Mirjana Lulic-Botica
Neonatal Clinical Specialist
Hutzel Women’s Hospital
(last update 04/04)

Objectives

- Discuss the frequency and causes of congenital malformations.
- Define human teratogenesis.
- Discuss the mechanisms of drug transfer across the placenta and list the factors which influence drug transfer.
- Review the FDA pregnancy drug risk categories.

Objectives

- Discuss the changes of drug categories through the three trimesters of pregnancy.
- Discuss the criticisms of the current drug risk categories.
- Identify drugs which are absolutely contraindicated in pregnancy/breastfeeding.
- Describe the pathophysiology and drug influences of human milk production.

Objectives

- List the factors which influence drug transfer into human milk.
- Review the lactation drug categories.
- Develop guidelines for selecting drugs for use in pregnant and lactating women.

Congenital Malformations

- Frequency
  - Severe congenital malformations occur in 3% of births.
  - Extrapolates to 120,000 newborns born in the US with severe birth defects.

Causes of Congenital Malformations

- Unknown 65-75%
- Genetic 15-25%
  - Autosomal/Sex-linked genetic disease
  - Cytogenetic (chromosomal)
- Environmental 10%
  - Maternal conditions 4%
  - Infectious agents 3%
  - Mechanical problems 1-2%
  - Chemicals/Rx drugs/Radiation <1%
Human Teratogenesis
- Defined as structural or functional dysgenesis of the fetal organs.
  - Congenital malformations can vary in severity resulting in:
    - IUGR
    - Carcinogenesis
    - Fetal demise

Placental barrier?
- There is really NO placental barrier that protects the embryo.
- MOST drugs and chemicals cross the placenta.

Physiologic changes in pregnancy affected pharmacokinetics
- 1) Decreased GI motility
- 2) Decreased plasma albumin concentration
- 3) Increased plasma and extracellular fluid volumes
- 4) Increase in renal elimination
- 5) Variation in uterine blood flow

Factors influencing transplacental transfer of medications
- Properties of placenta
- Maternal drug concentration and duration
- Concentration gradient between fetal/maternal blood
- Properties of medication
- Fetal circulation

Mechanisms of placental drug transfer
- Lipid solubility > Water solubility
- Un-ionized > Ionized
- Small > Large molecule
- Maternal & fetal blood pH
- Protein binding
- Placental blood flow
- Placental metabolism
- Maternal drug concentration

Principles of Drug Use in Pregnancy
- No drug should be considered 100% safe
- Indication for need should be present
- Weigh potential benefit against possible harm
- Understand the drug metabolism changes in pregnancy
Principles of Drug Use in Pregnancy
- Drugs may have different effect on fetus
- Drug effects may last longer on the fetus
- Drugs may have delayed fetal effect

FDA Classification – Tertogenic risk of drugs
- Category A
  - Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester (and there is no evidence of a risk in later trimesters) and the possibility of fetal harm appears remote.

FDA Classification – Teratogenic risk of drugs
- Category B
  - Either animal reproduction studies have not demonstrated a fetal risk, but there are no controlled studies in pregnant women OR animal reproduction studies in women in the first trimester (and there is no evidence of a risk in later trimesters).

FDA Classification – Teratogenic risk of drugs
- Category C
  - Either studies in animals have revealed adverse effects on the fetus (teratogenic, embrycidal, or other) and there are no controlled studies in women OR studies in women and animal studies are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus.

FDA Classification – Teratogenic risk of drugs
- Category D
  - There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (ex: drug needed in life-threatening situation or serious disease).

FDA Classification – Teratogenic risk of drugs
- Category X
  - Studies in animals or human beings have demonstrated fetal abnormalities or there is evidence of fetal risk based upon human experience or both, and the risk of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.
Drug risk categories changes of pregnancy trimesters

- Drug pregnancy risk category is sometimes NOT the same during the course of a pregnancy
- Therefore what may not be safe in the first trimester may be considered safe to use in the 2nd or 3rd trimester

Drugs Contraindicated during Pregnancy

- ACE inhibitors
- Androgenic hormones
- Busulfan
- Carbamazepine
- Chloramphenicol (3rd trimester)
- Coumarin derivatives
- COX-2 inhibitors

Examples if this include:

- ACE inhibitors:
  - No effect in the first trimester but may cause fetal hypotension syndrome in 2nd and 3rd trimester resulting in fetal kidney hypoperfusion, anuria, oligohydramnios, pulmonary hypoplasia and cranial bone hypoplasia.

Criticisms of current drug risk categories

- Disclaimer "Safe use in pregnancy has not been established" can imply that at medication may indeed be a teratogen.

Convey an incorrect impression that there is a gradation of reproductive risk from drug exposure across categories (i.e. that risk increases from A to B to C to D to X)

Convey an incorrect impression that the drugs within a category present similar reproductive risks

Drugs Contraindicated during Pregnancy

- Cyclophosphamide
- Diethylstilbestrol
- Ethyl alcohol
- Illicit drugs: cocaine, marijuana, crack, amphetamines etc.
- Isotretinoin
- Lithium
- Methotrexate
- Minoxidil
**Drugs Contraindicated during Pregnancy**
- Misoprostol
- NSAIDS
- Phenytoin
- Retinoids
- Tetracyclines
- Thalidomide
- Trimethoprim (1st trimester)
- Valproic Acid
- Warfarin (1st and 3rd trimester)

**Physiology of Lactation**
- Mammary gland synthesizes milk
  - Specialized alveolar cells
    - Create and control milk production
  - Specialized myoepithelial cells
    - Surround alveolar cells and ducts
    - Control milk let down
  - Ductule system
    - Drain alveoli; small ducts coalesce into main ducts that open directly onto nipple

**Factors which influence drug transfer in human milk**
- Passive diffusion
- Carrier-mediated/Active Transport
- Ion-tapping

**Drug factors favoring transfer**
- Unionized state
- High lipid solubility
- Low protein binding
- Weak Base
- Low molecular weight
- Maternal serum concentrations
- Milk composition - pH
- Infant feeding behaviors
- Drug factors

**Lactation drug categories**
- Dr Thomas Hale, "Medications and Mothers' Milk" has developed lactation risk categories.

**Lactation Risk Categories**
- L1 (Safest)
  - Drugs which have been taken by a large number of breastfeeding moms without any observed increase in adverse effect to the neonate OR
  - Controlled studies in the breastfeeding mother failed to demonstrate a risk to the infant OR
  - The medication is not orally bioavailable in an infant.
Lactation Risk Categories

- **L2 (Safer)**
  - Drugs which have been studied in a limited number of breastfeeding mothers without an increase in adverse effects.

- **L3 (Moderately safe)**
  - No controlled studies in breastfeeding mothers, however the risk of untoward effect to a breastfed infant is possible OR
  - Controlled studies show only minimal non-threatening adverse effects. Drugs should be given only if the potential benefit justifies the potential risk to the infant.

- **L4 (Possibly Hazardous)**
  - Positive evidence of risk to a breastfed infant, but the benefits from use in the breastfeeding mother may be acceptable despite the risk to the infant.

- **L5 (Contraindicated)**
  - Studies in breastfeeding mothers have demonstrated that there is significant and documented risk to the infant.
  - The risk of using the drug in breastfeeding mothers clearly outweighs any possible benefit from breastfeeding.

Guidelines for selecting drugs in the nursing mother

- Determining drug absorption from GI tract.
- Review theoretical infant dose and compare to known pediatric dose (dose less than 10% is considered safe).
- Choose drugs with shorter half-life.
- Be cautious of drugs and their active metabolites.
- Choose drugs with higher protein binding.

- Determine Relative Infant Dose (RID)
  - \[ \text{RID} = \frac{\text{Infant dose (mg/kg/day)}}{\text{Maternal dose (mg/kg/day)}} \]
  - A relative infant dose of <10% is generally considered safe.
Drugs Contraindicated during breastfeeding

- Amlodarone
- Antineoplastic drugs
- Cyclophosphamide
- Chloramphenicol
- Ergotamine
- Gold salts
- Illicit drugs
  - Amphetamines
  - Cocaine
  - Heroin
  - Marijuana

Drugs Contraindicated during Breastfeeding

- Lithium
- Radiopharmaceuticals
- Retinoids
- Tetracyclines
- Pseudoephedrine (may inhibit prolactin milk production)

Teratogen Information Services

- United Kingdom
  - National Teratology Information Service (NTIS)
    - Newcastle (191) 232 1525
- United States
  - Organization of Teratology Information Services
    - Utah (801) 328 2229
- Canada
  - Motherisk Program
  - Toronto (416) 813 6780

Questions?
5/27/04

From: Marianne Lulic-Botica, Neonatal Clinical Specialist

To: Pharmacy Staff

RE: Emergency Medication Box in MSCU pyxis

Please be informed that there is an emergency medication box in the MSCU pyxis unit. This box is intended to provide immediate access, under the direct supervision of the physician, of emergency medications in response to emergent conditions of the patient in the maternal special care unit.

The emergency medication box is stored in the pyxis unit and a back-up box is located in the neonatal area under the label printers. This emergency box is blue in color and labeled as “Emergency Med Box in the MSCU”.

The anticipated use of this medication box will be low. Once a box has been used, pharmacy will be notified by the nursing staff and a replacement box will need to be delivered on the next scheduled pharmacy technician run. Opened boxes will need to be restocked and medications used will need to be charged to the patient. This will be the responsibility of the neonatal technician.

Each emergency medication box must include:

1) Clearly labeled “Emergency Med Box for MSCU”
2) Content list on outside of box
3) Expiration date of first medication to expire
4) Charge slip
5) Medication content list containing expiration dates and dosing guideline inside the box.

Please note that Methergine® is referred to in the dosing guidelines but must be obtained from the refrigerator due to a short 2 week expiration dating at room temperature.

Please feel free to contact me with any questions and or concerns.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparation</th>
<th>Dosing Regimen</th>
<th>Maximum Dose / Rate / Comments</th>
</tr>
</thead>
</table>
| Furosemide(5 vials) (Lasix®) | 10 MG /ML  
4 ML VIAL | AS ORDERED PER PHYSICIAN                            | -potential aggravation of volume depletion and generally avoided in OB population  
- special indications in renal/cardiac disease                                                   |
| Labetalol(2) (Normodyne®)  
(Trandate®)                  | 5MG/ML  
20 ML VIAL | **HTN Emergencies:**  
20mg slow IVP x1 then  
40-80mg slow IVP q10min until desired BP is achieved.  
**MAX DOSE 300mg**  
**Continuous infusion:**  
0.5-2mg/min up to max dose of 300mg  
Administer IVP over 2-3 min. Max IVP rate of 2mg/min  
Max dose: 300mg  
Avoid in Asthma/CHF |                                                                   |
| Metoprolol (4) (Lopressor®) | 5MG/5ML  
5ML VIAL | AS ORDERED PER PHYSICIAN                            |                                                                                               |
| Hydralazine (Apresoline®) (5) | 20mg/ml  
1ml vial | **HTN Emergencies:**- adult - 5  
- 20 mg every 20 minutes until BP under control then q3-4 hours prn  
**Hypertension** - adult - give 5-20 mg /dose every 4 hours as needed  
Rapid IVP over 1-2 minutes  
Do not exceed 0.2mg/kg/min | **1st line agent for acute severe hypertension in preeclampsia**  
**IM route preferred**  
If given IV for life threatening emergency, administer over 1 minute and monitor BP closely |
| Methylergonovine(2) (Methergine®) | 0.2 MG/ML  
1ml vial | 0.2mg IM  
May repeat q2-4hr prn  
MAX 5 doses  
**IM route preferred**  
If given IV for life threatening emergency, administer over 1 minute and monitor BP closely |                                                                   |
| Calcium Gluconate(1)        | 1gram/10ml  
(100mg/ml)  
Route - IVP | 500-800 mg (MAX 3G/dose)  
MAX 50-100mg/min  
Repeat dose in 10 min if necessary |                                                                   |
| Oxytocin (2) (Pitocin®)     | 10 Units/ml  
1ml | 20 units/1000 ml IV infusion  
**titrate per policy** |                                                                   |
<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength</th>
<th>Quantity</th>
<th>Expiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium Gluconate</td>
<td>1 gram/10ml (100mg/ml)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Furosemide (Lasix®)</td>
<td>10mg/ml 4ml</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Hydralazine (Apresoline®)</td>
<td>20mg/ml 1ml</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Labetalol (Normodyne®, Trandate®)</td>
<td>5mg/ml 20ml</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Methylergonovine (Methergine®)</td>
<td>0.2mg/ml 1ml</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Metoprolol (Lopressor®)</td>
<td>5mg/5ml 5ml</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Oxytocin (Pitocin®)</td>
<td>10 Units/ml 1ml</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>
Review of OB/GYN population

Mojana Lulic-Kotica RPh
Neonatal Clinical Specialist
Hutzel Woman's Hospital

Objectives

1) Review of common medical abbreviations
2) Provide information on Hutzel nursing units
3) Discuss how to properly handle transfer orders

Objectives

4) Review of pharmacokinetics in the OB/GYN population
5) Review of anticoagulation the OB/GYN population

Objectives

6) Review of common disease states in the OB/GYN population:
   - HELLP syndrome
   - Gestational Diabetes
   - Rh incompatibility
   - Placental abruption
   - Tocolytics

Objectives

7) Review of commonly used medications in the OB/GYN population

Abbreviations

See attached table for most common abbreviations

Examples:
- IU/P at 36 4/7 wk GA based on LMP/US
- C-sect to NRFHT
- PPROM at 30 2/7wk GA
- 1 LTCS
- Pt is a 28yo G3P1112
Hutzel Nursing Units

- 3BS is a GYN unit. Patient may have GYN condition or present for early pregnancy termination. Ophthalmology and GYN plastic surgery also admit to this unit. Overflow patients may be admitted to 2BS bariatric floor.
- 2WN & 2WS are post-partum mother/baby units.
- 3BN is antenatal high-risk pregnant patients.
- 3WN is a LDR (labor, delivery, recovery) unit.

Hutzel Nursing Units

- MSCU (location 3WS) is a maternal ICU. Patient may be pregnant or post-partum.
- OBRR (location 3WS) Sometimes post-op antibiotics are started here especially if post-partum floors are full. Has no tube. Must tube to the MSCU tube station.
- 3WS-OR has C-section OR suites.
- 3WS is LDRP (labor, delivery, recovery, post-partum/mother/baby. Mother and baby stay in the same room for entire stay.

Hutzel Nursing Units

- 3BN – Shares 3BS tube station
- LRC – Labor Reception Area
- TRN – Transition Nursery. Also called A&J (Admission & Observation nursery)
- SCN – Special Care Nursery (formerly PCN) (2BC)
- NICU – Neonatal Intensive Care Unit (3BC)

Transfer orders – Adults

- New orders are required as patients transfer from unit to unit.
- Medications NOT rewritten on transfer order need to be discontinued.
- New orders are rewritten post partum. Medications NOT rewritten are to be discontinued.

Transfer orders – Neonates

- New orders are required as patients transfer from unit to unit.
- New orders are written when babies are transferred between each unit and between each phase of SCN (SCN, SCNN, SCNB) (Phase I, II and III).

Medication Emergency Box in MSCU

- Emergency box which is located in pyxis unit in MSCU
- Policy in progress
- Pharmacy to do exchange
- Back up boxes in neonatal area
- Meds include: Furosemide, Labetalol, Metoprolol, Hydralazine, Methergine, Calcium Gluconate, Oxytocin
Pharmacokinetics in OB/GYN population

- **Key Questions**
  - Is the patient pregnant? If so, how many weeks?
  - If post-partum, how long ago was the delivery?
  - Is this a GYN patient or an early pregnancy termination?

Pharmacokinetics in OB/GYN population

- **DMC antimicrobial guidebook** for DMC aminoglycoside (ag) pharmacokinetic equations: Ke, Clcr, IBW, adjusted BW, Vd.
- Clcr calculated - use IBW. If TBW < IBW use TBW.
  - if age > 65, use minimum Scr = 1.0
  - if age > 65, use minimum Scr = 0.8
- b. Vd = 0.3 L/kg
- Use TBW per DMC guidebook.
- Note: IBW is used by several computer dosing tools.
- If TBW > 30% over IBW, use AdjBW.
- (Acceptable to use AdjBW if TBW > 20% over IBW).

Pharmacokinetics in OB/GYN population

- **GYN patients:** Vd = 0.3 L/kg
- **Obstetric patients:**
  - Pre-partum: 1st trimester (<=16 wks), Vd = 0.3 L/kg
  - 2nd trimester (17-32 wks), Vd = 0.35 L/kg
  - 3rd trimester (33 wks thru delivery), Vd = 0.4 L/kg
- Post-partum: < 48 hrs post-partum, Vd = 0.4 L/kg
- > 48 hrs post-partum, Vd = 0.3 L/kg
- Vd chosen is based on when antibiotics are initiated.

Pharmacokinetics in OB/GYN population

- **High-Peak ODA Goals for Levels:**
- DMC exclusion is pregnancy
- Patients who present for early pregnancy termination may be dosed by ODA.
- Traditional Dosing
  - Used during pregnancy and labor & delivery
  - Usually requires q8hr interval due to rapid

Pharmacokinetics in OB/GYN population

- **DMC antimicrobial guidebook** for DMC aminoglycoside (ag) pharmacokinetic equations: Ke, Clcr, IBW, adjusted BW, Vd.
- Clcr calculated - use IBW. If TBW < IBW use TBW.
  - if age > 65, use minimum Scr = 1.0
  - if age > 65, use minimum Scr = 0.8
- b. Vd = 0.3 L/kg
- Use TBW per DMC guidebook.
- Note: IBW is used by several computer dosing tools.
- If TBW > 30% over IBW, use AdjBW.
- (Acceptable to use AdjBW if TBW > 20% over IBW).

- **DMC antimicrobial guidebook** for DMC aminoglycoside (ag) pharmacokinetic equations: Ke, Clcr, IBW, adjusted BW, Vd.
- Clcr calculated - use IBW. If TBW < IBW use TBW.
  - if age > 65, use minimum Scr = 1.0
  - if age > 65, use minimum Scr = 0.8
- b. Vd = 0.3 L/kg
- Use TBW per DMC guidebook.
- Note: IBW is used by several computer dosing tools.
- If TBW > 30% over IBW, use AdjBW.
- (Acceptable to use AdjBW if TBW > 20% over IBW).

- **DMC antimicrobial guidebook** for DMC aminoglycoside (ag) pharmacokinetic equations: Ke, Clcr, IBW, adjusted BW, Vd.
- Clcr calculated - use IBW. If TBW < IBW use TBW.
  - if age > 65, use minimum Scr = 1.0
  - if age > 65, use minimum Scr = 0.8
- b. Vd = 0.3 L/kg
- Use TBW per DMC guidebook.
- Note: IBW is used by several computer dosing tools.
- If TBW > 30% over IBW, use AdjBW.
- (Acceptable to use AdjBW if TBW > 20% over IBW).

- **DMC antimicrobial guidebook** for DMC aminoglycoside (ag) pharmacokinetic equations: Ke, Clcr, IBW, adjusted BW, Vd.
- Clcr calculated - use IBW. If TBW < IBW use TBW.
  - if age > 65, use minimum Scr = 1.0
  - if age > 65, use minimum Scr = 0.8
- b. Vd = 0.3 L/kg
- Use TBW per DMC guidebook.
- Note: IBW is used by several computer dosing tools.
- If TBW > 30% over IBW, use AdjBW.
- (Acceptable to use AdjBW if TBW > 20% over IBW).

- **High-Peak ODA Goals for Levels:**
- DMC exclusion is pregnancy
- Patients who present for early pregnancy termination may be dosed by ODA.
- Traditional Dosing
  - Used during pregnancy and labor & delivery
  - Usually requires q8hr interval due to rapid

- **DMC antimicrobial guidebook** for DMC aminoglycoside (ag) pharmacokinetic equations: Ke, Clcr, IBW, adjusted BW, Vd.
- Clcr calculated - use IBW. If TBW < IBW use TBW.
  - if age > 65, use minimum Scr = 1.0
  - if age > 65, use minimum Scr = 0.8
- b. Vd = 0.3 L/kg
- Use TBW per DMC guidebook.
- Note: IBW is used by several computer dosing tools.
- If TBW > 30% over IBW, use AdjBW.
- (Acceptable to use AdjBW if TBW > 20% over IBW).

- **High-Peak ODA Goals for Levels:**
- DMC exclusion is pregnancy
- Patients who present for early pregnancy termination may be dosed by ODA.
- Traditional Dosing
  - Used during pregnancy and labor & delivery
  - Usually requires q8hr interval due to rapid
Pharmacokinetics in OB/GYN population

- Guidelines for Levels:
  - Levels may be ordered after 3rd dose (day #3 of therapy) if not clinically improving or decreased renal function if therapy is to be continued.
  - Levels may be repeated – every 7 days

- Monitoring consideration for GYN plastic patients:
  - Serum Creatinine 3 times weekly
  - Use caution when selecting goals for levels i.e. treatment vs. prophylaxis
  - Check levels every 7 days

Vancomycin in OB/GYN

- Use DMC vancomycin nomogram if possible
- Common perinatally transmitted infection:
  - Group B streptococcus (GBS)
    - Vancomycin used for prophylaxis during labor & delivery for GBS positive or status unknown in patients with severe penicillin allergy; MUST be discontinued after delivery.
    - Std dose: Vancomycin 1 G IV PB q12 until delivery

Vancomycin documentation

- Documenting use of Criteria-Monitored Antimicrobials
- Vancomycin
  - PG (11) Intrapartum prophylaxis for Group B Streptococcal-positive or status unknown with severe penicillin allergy when use of alternative agents is precluded due to susceptibilities and/or allergy

Anticoagulation in the pregnant patient

- Pregnancy alone increases the risk of venous thrombosis five-fold and is the leading cause of maternal deaths
- Hypercoagulable state of pregnancy accounts for this increased risk and is related to increases in clotting factors, increase in venous stasis, decreases in natural inhibitors of coagulation and complications from the delivery itself such as placental abruption, infection and cesarean sections
Anticoagulation in the pregnant patient

- Anticoagulation is required for:
  1. Treatment of acute events
  2. Prophylaxis of patients with a history of thrombotic event
  3. Valvular heart disease
  4. Acquired Antiphospholipid syndrome
  5. Inherited Factor V Leiden, Protein C, Protein S, Antithrombin III, Prothrombin 20210 mutation
  6. Short course Heparin treatment for post-partum treatment of septic pelvic thrombosis

- Four potential approaches
  1. Warfarin throughout pregnancy (widely used in Europe but NOT in the US)
  2. Adjust – dose SC UFH throughout pregnancy
  3. Maintain mid-interval aPTT > 2x normal
  4. LMWH use throughout pregnancy
  5. Maintain a 4h post-dose anti-Xa level approx. 10 unit/ml
  6. UFH or LMWH until the 13th week, change to warfarin until the middle of the 3rd trimester, then restart UFH/LMWH until delivery.

LMWH use in pregnant women with prosthetic heart valve

- Low molecular weight heparins do not cross into fetal circulation
- Prophylactic doses may need to be adjusted secondary to pharmacokinetic changes.

Treatment of VTE during pregnancy

- Adjusted-dose sc Heparin is an alternative
- Adjust heparin doses to prolong a mid-interval aPTT into the therapeutic range
- Example: UFH 10,000 units sc q8h
- Check aPTT at 4h after the dose for target aPTT 48-78s

Placental drug transfer properties

- Lipid solubility > water solubility
- Un-ionized > Ionized
- Small > Large molecule
- Maternal & fetal blood pH
- Protein binding
- Placental blood flow
- Placental metabolism
- Maternal drug concentration

Maternal Testing - Serum Markers

- Biochemical markers which yield a risk assessment for open neural tube defects as well as trisomies 18 and 21.
- Maternal triple screen – performed at 16-18 weeks gestation
  - Alpha-fetoprotein
  - Unconjugated estriol
  - Human chorionic gonadotropin
Tests of Fetal Lung Maturity

- Lecithin:Sphingomyelin (L:S) ratio
  - Lecithin, a saturated phosphatidylcholine can be measured in amniotic fluid and is the principal active component of surfactant
    - L:S ratio >2:1 indicates mature lungs
    - L:S ratio 1.5-1.9 50% will develop RDS
    - L:S ratio <1.5:1 73% will develop RDS

Tests of Fetal Lung Maturity

- Phosphatidylglycerol
  - Marker for lung maturation late in pregnancy
  - Reported as absent or present

- TDx Fetal Lung Maturity
  - Measures the relative concentrations of surfactant and albumin
    - 30-70mg/g – Infant at risk for immature lungs
    - > 70mg/g – RDS risk is small

Maternal Testing

- Glucose Challenge Test
  - 24-48 weeks gestation

- Group B Streptococcus Test
  - 36 weeks gestation

- First trimester testing for:
  - Hepatitis B surface antigen, HIV status, RPR, Rubella, G/C

Maternal complications

- Pregnancy Induced Hypertension (PIH)
  - Affects 6-8% of pregnancies
  - Defined as BP > 140/90 mm Hg
  - Categorized by one of four conditions:
    - 1) Chronic hypertension th at pre dates pregnancy
    - 2) Preeclampsia-Eclampsia – elevated BP + proteinuria
    - 3) Chronic hypertension with su perimposed preeclampsia
    - 4) Gestational hypertension (nonproteinuric)

PIH

- Staging of Gestational HTN
  - Stage I hypertension: 140-159 mm Hg systolic a blood pressure and 90-99 mm Hg diastolic blood pressure;
  - Stage II: 160-179 mm Hg systolic and 100-109 mm Hg diastolic;
  - Stage III: 180-209 mm Hg systolic and 110-119 mm Hg diastolic;
  - Stage IV hypertension: systolic at 210 or greater and diastolic at 120 or greater.

PIH

- Treatment
  - Hydralazine
  - Methyldopa
  - Labetalol
  - Nifedipine
  - Magnesium
  - Avoid ACE inhibitors and Angiotensin receptor blockers due to fetal toxicity risks
Maternal complications

- Chorioamnionitis
  - Occurs in 1% of all deliveries
  - Commonly observed in prolonged labors and/or PROM
  - Results from ascending infection into the vagina then cervix and finally the uterine cavity, fetal membranes and placenta

Chorioamnionitis

- Signs and symptoms
  - Fever
  - Tachycardia (HR >120bpm)
  - Fetal tachycardia (>160 bpm)
  - Purulent or foul-smelling fluid/vaginal discharge
  - Uterine tenderness
  - Maternal leukocytosis
  - Hypotension

Chorioamnionitis

- Risk to fetus
  - Risk of neonatal infection increases as the duration of ruptured membranes lengthens

- Treatment
  - Aminoglycoside + Clindamycin/Ampicillin

Maternal complications –

- Post-partum endometritis
  - Background
    - This is the most common postpartum infection. This infection is of the endometrium (lining) of the uterus. This lining is very vulnerable after the detachment of the placenta. It is more likely to occur post C-Section
  - Signs and symptoms
    - Fever (as high as 105 degrees), vague lower abdominal pain, foul smelling vaginal discharge, chills, headache, general malaise

Post partum endometritis – treatment

- Treatment
  - Triple antibiotics most commonly used:
    - Amoxicillin 2g IVPB q8h
    - Gentamycin ODA dosing
    - Clindamycin 900mg IVPB q8

Post partum endometritis – treatment

- It is imperative that antibiotics be initiated immediately and that Gentamicin empirically initiated at appropriate doses
- Therapy is continued until patient is afebrile x48 hours
- Cultures should be obtained but are not always done routinely.
Maternal complications

- Gestational Diabetes (GD)
  - Diagnosis requires at least 2 abnormal plasma glucose values on a 3 hour oral glucose tolerance test (100g glucose)
    - Fasting \( \geq 105 \text{mg/dL} \)
    - 1hr \( \geq 190 \text{mg/dL} \)
    - 2hr \( \geq 160 \text{mg/dL} \)
    - 3hr \( \geq 145 \text{mg/dL} \)

Gestational Diabetes

- Earlier description of diabetic pregnancies relied on White’s classification.
- Today it is primarily used to compare groups of infants delivered
  - Nomenclature is based on age of onset, duration of disorder and complications

White’s classification

<table>
<thead>
<tr>
<th>CLASS</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Chemical diabetes with (+) GTT before/during pregnancy</td>
</tr>
<tr>
<td>2</td>
<td>Onset after age 20; 20 years duration</td>
</tr>
<tr>
<td>3</td>
<td>Onset at age 10-19</td>
</tr>
<tr>
<td>4D</td>
<td>Onset before age 10</td>
</tr>
<tr>
<td>4D2</td>
<td>Duration &gt;25 years</td>
</tr>
<tr>
<td>4D3</td>
<td>Calcification of vessels of the leg</td>
</tr>
<tr>
<td>4D4</td>
<td>Renal insufficiency</td>
</tr>
<tr>
<td>4D5</td>
<td>Hypertension</td>
</tr>
<tr>
<td>4E</td>
<td>Calcification of pelvic vessels</td>
</tr>
<tr>
<td>4F</td>
<td>Nephropathy</td>
</tr>
<tr>
<td>4G</td>
<td>Pregnancy failures</td>
</tr>
<tr>
<td>4H</td>
<td>Vascular lesion developed in childbirth neon mem. cardiopathy</td>
</tr>
<tr>
<td>4I</td>
<td>Malnutrition</td>
</tr>
</tbody>
</table>

Gestational Diabetes

- GDM is as a result of physiologic changes in maternal glucose utilization resulting in an inability to mount an appropriate insulin response
- This compromises the fetal environment due to exposure of high maternal glucose levels, episodic hypoglycemia and ketone exposure

Gestational Diabetes

- Pregnant women who develop GDM with or without superimposed Type I or Type II DM that are poorly controlled result in a fetal environment that can during the course of the pregnancy result in:
  - Congenital malformations
  - Fetal hyperglycemia
  - Fetal hyperinsulinism

Gestational Diabetes

- Goals for management include:
  - Good prenatal care
  - Obtaining good metabolic control before conception
  - Maintaining goal Hemoglobin A1c levels especially during the first trimester
    - Fasting capillary blood glucose level of \(<95-105\text{mg/dL} \)
    - Postprandial goal of \(<140\text{mg/dL} \)
Gestational Diabetes

**Treatment:**
- 1) Diet controlled
  - Monitoring of glucose levels at least 4 times daily
  - Postprandial testing is preferred
- 2) Insulin
  - No specific studies declaring one type of insulin or a certain regimen as superior
  - Common initial dose:
    - 0.7 units/kg/day (2/3 qam & 1/3 qpm of which 1/3 of dose is regular insulin and 2/3 as NPH)

Maternal complications

- HELLP syndrome is characterized by hemolysis, elevated liver enzyme levels and a low platelet count
- Occurs in 0.2-0.6% of pregnancies
- 4-12% of patients with preeclampsia develop superimposed HELLP
- Considered to be a variant of preeclampsia

HELLP

- Pathogenesis of HELLP remains unclear
- Early diagnosis is critical due to reported high morbidity and mortality rates as high as 25%

HELLP

- Therapy includes:
  - Supportive management
    - Seizure prophylaxis
    - Blood pressure control
    - Blood products transfusion as required
    - Corticosteroid therapy
    - Plasmapheresis for refractory HELLP syndrome

- Pathogenesis of HELLP is not well understood
  - Multisystem disease attributed to abnormal vascular tone, vasospasm and coagulation defects
  - Syndrome seems to be the final manifestation of some insult that leads to microvascular endot heli el damage and intravascular platelet activation
  - Platelet activation - Thromboxane A + Serotonin release - vasospasm - platelet aggregation - further endothelial damage
HELLP

- Diagnostic tests:
  - Hct (last of three abnormalities to occur)
    - Decreased serum haptoglobin level may confirm ongoing hemolysis when Hct is normal
  - Liver enzymes
  - Platelets
  - Proteinuria
  - Uric acid – increased concentration in HELLP

- Treatment
  - Antihypertensives:
    - Hydralazine 2.5-5mg IV and titrate
    - Labetaol
    - Nifedipine
  - Magnesium sulfate
  - Corticosteroids
    - Dexamethasone up to 10mg IV q12

Maternal complications – Rh Incompatibility

- Isoimmune hemolytic anemia when Rh-negative mother previously sensitized to the Rh (D) antigen and her Rh-positive fetus
- Placental transfer of maternal immunoglobulin G (IgG) – Rh antibody
- Rh/ABO incompatibilities

Maternal complications

- Preterm delivery affects 1 in 10 births and is the cause of at least 75% of neonatal deaths

Premature labor

- Risk factors:
  - Maternal – low socioeconomic status, race, maternal age (<18, >40), smoking, substance abuse, hx of preterm delivery, hx of a second trimester abortion
  - Uterine factors – increases in uterine volume, uterine anomalies, trauma
  - Infection – Neisseria gonorrhoeae, Chlamydia, Treponema pallidum, Trichomonas vaginalis, Gardnerella vaginalis, GBS

Premature labor

- Biochemical markers
  - Fibronectin
  - Cytokine (Interleukin-6)
  - Estradiol-178
  - Estriol
  - Progesterone
Premature labor

- Signs and Symptoms
  - Frequent contractions (>4 per hour)
  - Cramping
  - Pelvic pressure
  - Excessive Vaginal discharge
  - Backache/low back pain

Premature labor

- Management
  - Corticosteroids
    - Only treatment shown to improve fetal survival
    - Pred 12mg IM q12 x2 doses OR
    - Dexamethasone 5mg IV q12 x4 doses
  - Antibiotics (erythromycin/clindamycin)
  - Emerging Treatments
    - Oxytocin inhibitors
    - Atosiban
    - Nonpeptide oxytocin antagonist

Commonly used medications in OB/GYN population

- Oxytocin (Pitocin®)
  - MOA: Oxytocic agent which produces rhythmic uterine contractions during the induction or augmentation phase of labor.
  - INDICATION:
    - Stimulates the induction of uterine contractions before they begin on their own

Oxytocin

- Reasons for the induction of labor include:
  - Fetal
    - IUGR
    - Lack of amniotic fluid
    - Severe Rh disease
  - Fetal compromise
  - Augmentation to support contractions to help labor progress
  - Maternal:
    - Labor is weak/erotic/stalled
    - Fetal:
    - Fetal compromise
    - Control post-partum bleeding

Commonly used medications in OB/GYN

- Maternal:
  - PROM at term
  - Pregnancy past the estimated due date 7-14 days
  - Uncontrolled maternal diabetes – deterioration of placenta or baby thought to be large
  - Uncontrolled pregnancy induced hypertension – preeclampsia
  - Chronic illness – SLE, Sickle cell, Chronic renal insufficiency
Commonly used medications in OB/GYN

- Fetal
  - IUGR
  - lack of amniotic fluid
  - Severe Rh disease
  - Fetal compromise
- Augmentation to support contractions to help the labor progress
- Maternal:
  - Labor is weak/erratic/stalled
- Fetal:
  - Fetal compromise
- Controls post-partum bleeding

Commonly used medications in OB/GYN

- Rate of Drip standard bag of 2 units of Oxytocin/100ml of IV fluid:
  - 10gts = 1 ml
  - 0.5 mu/min = ½ gtt/min = 3 ml/hr
  - 1 mu/min = 1 gtt/min = 6 ml/hr
  - 2 mu/min = 2 gtt/min = 12 ml/hr
  - etc.
- Rate of Drip of standard bag of 10 units of Oxytocin/500ml of IV fluid
  - 0.5 mu/min = 1.5 ml/hr
  - 1 mu/min = 3 ml/hr
  - 2 mu/min = 6 ml/hr
  - etc.

Commonly used medications in OB/GYN

- Rho(D) Immune Globulin (Rhogam®)
- MOA: Suppresses the immune response and antibody formation of Rh-negative individuals to Rh-positive red blood cells.
- Indication
  - Prevention of iso-immunization in Rh-negative mother exposed to Rh-positive blood during delivery of an Rh-positive infant to prevent haemolytic disease of the newborn.
- Contraindications
  - Any hypersensitivity to immune globulins, transfusion of Rho(D)-positive blood in previous 3 months

Commonly used medications in OB/GYN

- Dosing
- Antepartum prophylaxis:
  - At 28 weeks in-utero gestation: 300 mcg Rhogam IM x1
  - Repeat within 72 hours of delivery:
  - (Dose also administered post miscarriage/abortion/amniocentesis/bleeding) 300 mcg Rhogam IM x1

Postpartum bleeding:
- 10 Units Oxytocin IM after delivery
- 10-40 Units Oxytocin/1000ml of IV fluid given IV
Commonly used medications in OB/GYN population

- **Antepartum treatment:**
  - If the pregnant women has previously developed Rh antibodies:
  - Anti-D IgG may be given to check blood type of the fetus. If it is Rh positive, the maternal antibodies are monitored regularly.
  - If the antibody levels become dangerously high, a transfusion or Rh negative blood may be necessary.
  - In most severe cases of incompatibility, a transfusion while fetus is still in uterus.
  - If the fetal packed red blood cell volume that has entered the maternal circulation is <15 ml: Administer 300 mcg (1 vial) IM x 1.
  - 8 vials reg = RBC volume of the calculated fetomaternal hemorrhage divided by 15ml

Commonly used medications in OB/GYN populations

- **Post miscarriage/abortion/termination of ectopic pregnancy:**
  - 50 mcg IM x 1 within 3 hours but not later than 72 hours if <13 weeks of gestation
  - 300 mcg IM x 1 within 3 hours but not later than 72 hours if >13 weeks of gestation

Commonly used medications in OB/GYN population

- **Methotrexate**
  - MOA:
  - An antimetabolite, which inhibits DNA synthesis and cell production in malignant cell/ectopic pregnancies
  - **Indication**
  - Ectopic Pregnancy: Fertilized egg which has implanted outside the uterus usually in the fallopian tubes (97%)
  - Interstitial Pregnancy: Fertilized egg which has implanted at highly vascular region of uterus near insertion of fallopian tubes – egg can grow larger than those within fallopian tubes

Commonly used medications in OB/GYN population

- **Dosing**
  - Ectopic pregnancy:
    - 50mg/2.5mg single dose without leucovorin rescue
    - Maximum 1000mg dose = 4 ml which should be divided as 2 separate injection sites of 2ml each.
  - Interstitial pregnancy:
    - Methotrexate 1mg/kg IM qd x 4 does total (Day 1,3,5,7)
    - PLUS
    - Leucovorin 0.1mg/kg PO/M x 4 doses on alternating days (Day 2,4,6,8) (Homocysteine)
    - (Leucovorin acts as an RBC acid antagonist as rescue therapy post MTX treatment)

Commonly used medications

- **Misoprostol**
  - Induction/Cervical Ripening
    - 25-50 mcg intravaginally q3-6hr or 100mcg PO q3-6hr
  - Termination
    - 200-800mcg PO/Intravaginally q3-6hr
Commonly used medications

- Prostaglandin gels
  - Compounded by the pharmacy 2mg/5ml for up to 3 doses

Questions?
Pharmacokinetic Dosing in the OB/GYN population
(last updated 03/05 by M. Lulic-Botica and S. Burns)

Key Questions
- Is the patient pregnant? If so, how many weeks?
- If post-partum, how long ago was the delivery?
- Is this a GYN patient or an early pregnancy termination?

1. Refer to DMC Antimicrobial Formulary and Clinical for pharmacokinetic equations:

- **GYN patients**: Vd = 0.3 L/kg

- **Obstetric patients**:
  - Pre-partum: 1st trimester (<=16 wks), Vd = 0.3 L/kg
  - 2nd trimester (17-32 wks), Vd = 0.35 L/kg
  - 3rd trimester (33 wks thru delivery), Vd = 0.4 L/Kg
  - Post-partum: <48 hrs post-partum, Vd = 0.4 L/kg
  - >48 hrs post-partum, Vd = 0.3 L/kg

Vd chosen is based on when antibiotics are initiated

Dosing of aminoglycosides in the laboring patient prior to delivery
- Patients that spike a temperature prior to delivery are suspected to have chorioamnionitis and are initiated on:
  - Gentamicin 2mg/kg IVPB x1 then 1mg/kg IVPB q8hr until delivery
  - This dosing is generally adequate if anticipated delivery is short.
  - However if labor is prolonged or mother is extremely obese, pharmacokinetic calculating will be required for desired peak of 6-8 mg/L and trough less than 1 mg/L

Doses do NOT need to be automatically changed at 3 days if the initial Vd chosen was 0.4L/kg. Most patients will continue on antibiotics only until afebrile x48 hours. For those patients that continue or are not clinically improving on the 3rd day, consider levels. The level will then support the dose or the need to change it.
- Round doses to nearest 20 mg even increments for gent/tobra.

- **High-Peak ODA Goals for Levels**:
  - DMC exclusion for pregnancy
  - Patients who present for early pregnancy termination may be dosed by ODA.

- **Traditional Dosing**
  - Used during pregnancy and labor & delivery
  - Usually requires q8hr interval due to rapid glomerular filtration rate during pregnancy.
Common OB/GYN condition:
- Endometritis, chorioamnionitis, PID, pyelonephritis, tubo-ovarian abscess (TOA)
- Gent/Tobra Peak Goals: ODA 12-16mg/L
- Traditional 6-8mg/ml
- Abscess not amenable to surgery should be dosed more aggressively: ODA 16-20mg/L

Guidelines for Levels:
- Levels may be ordered after 3rd dose (day #3 of therapy) if not clinically improving or decreased renal function if therapy is to be continued.
- Levels may be repeated approximately every 7 days

GYN plastic surgery patients are at risk for aminoglycoside toxicity secondary to:
- Multiple surgeries with multiple courses of therapy
- Long duration of treatment with aminoglycosides
- Urinary outflow obstruction often complicates GYN graft surgery

Monitoring consideration for GYN plastic patients:
- Serum Creatinine 3 times weekly
- Use caution when selecting goals for levels i.e. treatment vs. prophylaxis
- Check levels approximately every 7 days

Vancomycin in OB/GYN
- Use DMC vancomycin nomogram if possible
- Common perinatally transmitted infection:
  - Group B streptococcus (GBS)
    - Vancomycin used for prophylaxis during labor & delivery for GBS positive or status unknown in patients with severe penicillin allergy; MUST be discontinued after delivery.
    - Standard dose: Vancomycin 1 G IVPB q12 until delivery

Vancomycin documentation
- Documenting use of Criteria-Monitored Antimicrobials
  - Vancomycin
    - P9 Intrapartum prophylaxis for Group B Streptococcal-positive or status unknown with severe penicillin allergy when use of alternative agents is precluded due to susceptibilities and/or allergy.
To: Pharmacy Staff

From: Marianne Lulic-Botica, Clinical Pharmacy Specialist
     Greg Polk, Director Pharmacy Services

RE: STAT ORDERS FOR ZIDOVUDINE FOR PREGNANT PATIENTS IN ACTIVE LABOR

During the active phase of labor when the pregnant patient's membranes have ruptured (“water has broke”) and the patient is HIV positive, the single most important medication in terms of decreasing perinatal transmission to the baby is the prompt initiation of Zidovudine (Retrovir®, AZT). During this “active” phase of labor the fetus is potentially exposed to virus containing maternal genital secretions and blood. Contractions during labor result in the micro transfusion of blood from mother to fetus (approx. 3mL).

The overall risks of vertical transmission of the virus has improved in part due to better and earlier detection of the virus, the use of anti-retrovirals prenatally, treatment of zidovudine antenatally and the early initiation of zidovudine to the neonate.

The risk of perinatal transmission of virus to the baby is significantly reduced if antiretrovirals are promptly initiated. The exact timing of transmission to the baby is unknown but risk factors include low CD4 counts (<200 cells/mm³), rupture of membrane > 4 hours and preterm labor. Current evidence suggests that 30% of transmission occurs before birth and 70% at the time of delivery. Vertical transmission rates were significantly reduced when comparing mothers with no treatment vs. prenatal treatment, intrapartum treatment and neonatal zidovudine. (20% vs 3% respectively). The use of Zidovudine during pregnancy and delivery has become the standard of care in the United States.

**During active phase of labor:**
Zidovudine (Retrovir®) 2mg/kg (TBW) IVPB x1 STAT over 1 hour then
Zidovudine (Retrovir®) 1mg/kg/hr continuous drip STAT until delivery

**MS MEDS Fast Movers**
Access pathway 3 in MS MEDS. Select: Zidovudine bolus 2mg/kg IVPB
Insert calculated dose. In D5W 100ml. This bag does NOT have to be total volume.

Access pathway 3 in MS MEDS. Select: Zidovudine drip 1mg/kg/hr. Enter frequency code “q8h”. Bag will generally last approximately 8 hours.
Standard drip of 750mg Zidovudine = 75ml + 175 ml D5W for TV=250ml.
Special instructions on label:
Conc = 3mg/ml
Infuse 1mg/kg/hr = _________mg/hr = __________ ml/hr
Please treat these orders as STAT orders. Pharmacists, expect to take an initial verbal order in order to initiate the load dosing and continuous as quickly as possible. The resident or attending physician will call down with a patient name, current weight and location. These patients should already be registered and in the system with an account number but please confirm the patient unit. Medication orders will then be subsequently tubed to the floor. Please call the floor to inform the nursing staff that the medication has been sent.

Pharmacy technicians, please treat these orders as STAT. Zidovudine 10mg/ml 20 ml vials have been placed in one of the medication bins by the STAT IV Hood. Please tube medications immediately after preparation.

Please feel free to contact me with any questions or concerns at pager #6461. I thank you in advance for your cooperation.
Oxytocin (Pitocin®)

**MOA:** Oxytocic agent which produces rhythmic uterine contractions during the induction or augmentation phase of labor.

**INDICATION:**
- Stimulates the induction of uterine contractions before they begin on their own
  - Reasons for the induction of labor include:
    - Maternal:
      - PROM at term
      - Pregnancy past the estimated due date 7-14 days
      - Uncontrolled maternal diabetes - deterioration of placenta or baby thought to be large
      - Uncontrolled pregnancy induced hypertension - preeclampsia
      - Chronic illness- SLE, Sickle cell, Chronic renal insufficiency
    - Fetal
      - IUGR
      - lack of amniotic fluid
      - Severe Rh disease
      - Fetal compromise
  - Augmentation to support contractions to help the labor progress
    - Maternal:
      - Labor is weak/erratic/stalled
    - Fetal:
      - Fetal compromise
  - Controls post-partum bleeding
CONTRAINDICATIONS:

Absolute:
- Placenta previa (placental attachment to lower half of uterus covering, partially covering or touching the os (mouth of the uterus). The closer to the os, the greater the possibility of hemorrhage)
- Inadequate pelvis
- Tetanic contractions: contractions > 90 seconds
- Water intoxication (antidiuretic effect of oxytocin): confusion, lethargy, amnesia, convulsions

Relative
- NRFHT (Non-reassuring fetal heart tones)
- Active HSV infections
- Abnormal fetal positions - breach

MONITORING

Fetal:
- External of internal monitoring based on condition/situation
  - FHR
    o Baseline
    o Variability
    o Periodic/Non-periodic changes
    o Reassuring/Non-reassuring characteristics:
      ▪ Repetitive late heart rate decelerations
      ▪ Repetitive significant variable decelerations (FHR < 70BPM lasting 60 seconds)
      ▪ Prolonged FHR decelerations (FHR < 80 BPM lasting > 90 seconds)
      ▪ Fetal tachycardia (> 160 BPM for > 10min)

Maternal:
- Baseline vital signs, BP
- Monitor I/O
- Uterine Activity
  o Contraction pattern
  o Resting tonus
  o Frequency
  o Duration
  o Intensity
- Observe for uterine hyperstimulation
  o > 6 contractions in 10 min x2
  o Contractions > 90 seconds in duration
DOSING
Standard Bag:
10 Units of Oxytocin in 500ml/1000ml D5LR/LR

Induction:
Start Oxytocin at 1-2 mu/min and increase by 2 mu/min every 15-30 min until a desired contraction pattern has been established. Once the contraction pattern has been established and the labor has progressed to a 5-6cm dilation, the dose may be reduced by similar increments.
(Rates greater than 10 mu/min are rarely required). Contraction pattern includes:
- Contraction duration of 40-60 seconds
- Uterine palpitations indicate strong contraction
- Intrauterine Pressure Catheter shows an amplitude of 40-90 mmHg

Augmentation:
Start Oxytocin at 0.5-1 mu/min and increase by 1-2 mu/min every 15-30 minutes
Titrate to response

Rate of Drip standard bag of 10 units of Oxytocin/1000ml of IV fluid

<table>
<thead>
<tr>
<th>Dose (mu/min)</th>
<th>Drops/min</th>
<th>Rate/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>½</td>
<td>3ml/hr</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>6ml/hr</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>12ml/hr</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>18ml/hr</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>24ml/hr</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>30ml/hr</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>36ml/hr</td>
</tr>
<tr>
<td>7</td>
<td>7</td>
<td>42ml/hr</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>48ml/hr</td>
</tr>
<tr>
<td>9</td>
<td>9</td>
<td>54ml/hr</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>60ml/hr</td>
</tr>
</tbody>
</table>
### Rate of Drip of standard bag of 10 units of Oxytocin/500ml of IV fluid

<table>
<thead>
<tr>
<th>Dose (mu/min)</th>
<th>Drops/min</th>
<th>Rate/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>½</td>
<td>1.5ml/hr</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>3ml/hr</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>6ml/hr</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>9ml/hr</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>12ml/hr</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>15ml/hr</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>18ml/hr</td>
</tr>
<tr>
<td>7</td>
<td>7</td>
<td>21ml/hr</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>24ml/hr</td>
</tr>
<tr>
<td>9</td>
<td>9</td>
<td>27ml/hr</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>30ml/hr</td>
</tr>
</tbody>
</table>

**Postpartum bleeding:**

- 10 Units Oxytocin IM after delivery
- 10-40 Units Oxytocin/1000ml of IV fluid given IV
- Adjust rate to sustain uterine contraction and uterine atony
Rho(D) Immune Globulin (Rhophylac®)

**MOA:** Suppresses the immune response and antibody formation of Rh-negative individuals to Rh-positive red blood cells.

**Indication**
Prevention of iso-immunization in Rh-negative mother exposed to Rh-positive blood during delivery of an Rh-positive infant to prevent haemolytic disease of the newborn.

**Contraindications**
Any hypersensitivity to immune globulins, transfusion of Rho(D)-positive blood in previous 3 months

**Dosing**

*Antepartum prophylaxis:*
At 28 weeks in-utero gestation: 300mcg Rhophylac® IM x1
Repeat within 72 hours of delivery:
(Dose also administered post miscarriage-abortion/amniocentesis/bleeding)
300mcg Rhophylac® IM x1 *(Rhophylac® brand may also be given IV; Rhogam® brand may only be given IM).*

*Antepartum treatment:*
If the pregnant women has previously developed Rh antibodies:
- amniocentesis may be done to check the blood type of the fetus. If it is Rh positive, the maternal antibodies are monitored regularly.
- If the antibody levels become dangerously high, a transfusion or Rh negative blood may be necessary.
- The most severe cases of incompatibility may require fetal transfusion while fetus is still in uterus.

If the fetal packed red blood cell volume that has entered the maternal circulation is <15 ml: Administer 300mcg(1 vial ) IM x1
# vials req’d = RBC volume of the calculated fetomaternal hemorrhage divided by 15ml

*Post miscarriage-abortion/termination of ectopic pregnancy:*
50 mcg IM x1 within 3 hours but not later than 72 hours if <13 weeks of gestation
300mcg IM x1 within 3 hours but not later than 72 hours if >13 weeks of gestation
**Methotrexate**

**MOA**
An antimetabolite, which inhibits DNA synthesis and cell production in malignant cells/ectopic pregnancies

**Indication**
- Ectopic Pregnancy: Fertilized egg which has implanted outside the uterus usually in the fallopian tubes (97%)
- Interstitial Pregnancy: Fertilized egg which has implanted at highly vascular region of uterus near insertion of fallopian tubes - egg can grow larger than those within fallopian tube

![Sites and incidence of ectopic pregnancies](image)

**Signs & symptoms**
Spasmodic crampy pain with tenderness starting on one side and then spreading
Brown vaginal spotting/light bleeding
N&V
Dizziness
Weakness
Shoulder pain
Rectal pressure
If tube ruptures: bleeding is heavy and signs of shock are common

**Contraindications**
Hypersensitivity to Methotrexate, severe renal/hepatic impairment, blood dyscrasias, bone marrow suppression
**Monitoring**
hCG levels are monitored and expected to decrease

**Dosing**

**Ectopic pregnancy:**
50mg/m² IM single dose without leucovorin rescue
Maximum 100mg dose = 4 ml which should be divided as 2 separate injection sites of 2ml each.

**Interstitial pregnancy:**
Methotrexate 1mg/kg IM qod x 4 doses total (Day 1,3,5,7)

+ Leucovorin 0.1mg/kg PO/IM qod x 4 doses on alternating days (Day 2,4,6,8)
(Folinic acid)
(Leucovorin acts as a folic acid antagonist as rescue therapy post MTX treatment)

**Calculation of BSA:**
BSA (m²) = \( \frac{\text{Ht (inches)} \times \text{Wt (lbs)}}{3131} \)

**Side effects**
Reddening at injection site, N&V, diarrhea, fever, chills, blurred vision
Post-partum endometritis

Background
This is the most common postpartum infection. This infection is of the endometrium (lining) of the uterus. This lining is very vulnerable after the detachment of the placenta. It is more likely to occur post C-Section

Signs and symptoms
Fever (as high as 105 degrees), vague lower abdominal pain, foul smelling vaginal discharge, chills, headache, general malaise

Treatment
Triple antibiotics most commonly used:
Ampicillin 2g IVPB q6hr
Gentamicin high peak single daily: Dose = Vd(L/kg) x ABW(kg) x peak desired(mg/L)
  Vd = 0.4L/kg for 5-7 days post-partum, then use
  Vd = 0.3L/kg
  ABW= (TBW-IBW)(0.4) + IBW
  IBW(female) = 45.5kg + (2.3 x height in inches over 5 feet)
  Desired peak for endometritis: 12-16mg/l
Clindamycin 900mg IVPB q8

It is imperative that antibiotics be initiated immediately and that Gentamicin levels are adequate.
Therapy is continued until patient is afebrile x48 hours
Cultures should be obtained but are not always done routinely.