OB/GYN PEARLS

(Mirjana Lulic-Botica RPh and Steve Burns RPh)

(last updated 12/29/04)

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Anticoagulation Considerations in the Pregnant Patient

(last updated 12/04 by M. Lulic-Botica, Neonatal Clinical Specialist)

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 (APPT 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. Courmarin 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
I 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 Warfarain 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.

Cervical Ripening/Labor Induction Agents Comparison Chart(last updated 4/2003 by Mirjana Lulic-Botica RPh)

DRUG	DOSE	ROUTE	INTERVAL	MAX DOSE	ADVANTAGES	DISADVANTAGES	CONTRAINDICAT.	COST
Oxytocin (Pitocin®)	1-6 mU/min	IV	Increase dose in increments of 15-60min	25mU/min	-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	-anti-diuretic effect at high doses -uterine hyperstimulation -uterine rupture	-fetal distress -cephalopelvic disproportion -unfavorable fetal position -hyperactive uterus	Med: 0.39cents + IV + nursing time + pump Roughly estimated as $50-100
Prostaglandin gels (compounded from Dinoprostone 20mg Supp)	2mg/5ml	Intravaginal	Q6hr	3gels/24hr	-cost compared to commercially available Prepidil® and Cervidil®	-compounded by pharmacy -must be refrigerated	VBAC deliveries???? -cephalopelvic disproportion -hyperactive uterus -multipara >=6 -placental previa -vaginal bleeding -Vaginal delivery not indicated ex: HSV	$40
Misoprostol (Cytotec®)	25-50mcg	Intravaginal	Q4-6hr	6-8dose	-cost -convenience -no refrigeration required	-tachysystole - uterine hyperstimulation -higher incidence of meconium staining -uterine rupture -bioavailability of vag administration is 3x greater than oral administration	-VBAC deliveries -Previous infections -Hyperactive uterus	0.44 cents/0.1mg tab
Dinoprostone insert (Cervidil®)	10mg	Intravaginal	Vag insert x1 dose	One	-one time dose -constant release of medication @ 0.3mg/hr -inserted and removed more easily if uterine hyperstimulation occurs	-cost -uterine hyperstimulation -uterine rupture	VBAC deliveries??? -fetal distress -multipara >=6 -simultaneous IV oxytocin -vaginal bleeding -cephalopelvic disporportion	$175/insert
Dinoprostone gel (Prepidil®)	0.5mg gel	Intracervical	Q6hr	3gels/24hr	-commercially available gel	-cost -gels must be kept refrigerated -uterine hyperstimulation -uterine rupture	VBAC deliveries???? -cephalopelvic disproportion -hyperactive uterine -multipara >=6 -placental previa -vaginal bleeding -Vaginal delivery not indicated ex: HSV	$125/gel

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

COMMON OB/GYN/NEONATAL ABBREVIATIONS

(last updated by Mirjana Lulic-Botica RPh 3/24/04)

A/B	Apnea/Bradycardia
AB	Abortion
ABO	Blood types A, B and O
AF	Amniotic fluid
AFP	Alpha-fetoprotein
AFV	Amniotic fluid volume
AGA	Appropriate for gestational age
Amnio	Amniocentesis
ANA	Antinuclear antibody
AP	Ante-partum
APS	Anti-phospholipid syndrome
AROM	Artificial rupture of membranes
ASD	Atrial septal defect
BBT	Basal body temperature
BCP	Birth Control Pill
BHCG	Beta human chorionic gonadotropin
BM	Breast milk
BMZ	Betamethasone
BPD	Bronchopulmonary dysplasia
BPM	Beats per minute
BSO	Bilateral Salpingo-oophorectomy
BTL	Bilateral tubal ligation
BV	Bacterial vaginosis
CAH	Congenital adrenal hyperplasia
CD	Cesarean delivery
CHORIO	Chorioamnionitis
CMV	Cytomegalovirus
COA	Coarctation of aorta
Coomb's	Direct antiglobulin test
C-SECT or C/S	Cesarean section
CST	Contraction stress test
CST	Contraction stress test
CVS	Chorionic villus sampling
Cx	Cervix
D&C	Dilatation & Curettage
D&E	Dilatation & Evacuation
DFA	Direct fluorescent antibody
DHT	Dihydrotestosterone
ECMO	Extracorporeal membrane oxygenation
ECS	Endocervical scrape
EFW	Estimated fetal weight
ELBW	Extremely low birth weight

EmBx	Endometrial biopsy
ENNS	Early Neonatal neurobehavioral score
Epis Med.	Medial episiotomy
Epis LML	Left mediolateral episiotomy
Epis RML	Right mediolateral episotomy
Epis.	Episiotomy
FAS	Fetal alcohol syndrome
FBS	Fasting Blood Sugar
FBS	Fetal breathe sounds
FHR	Fetal heart rate
FHR-UC	Fetal heart rate- uterine contraction
FHT	Fetal heart tones
FT	Fetal tone
FT	Full term
FTA-ABS	Fluorescent treponemal antibody absorbd
FTD	Failure to descend
FTND	Full term normal delivery
FTP	Failure to progress
FTT	Failure to thrive
FUB	Functional uterine bleeding
FUO	Fever of unknown origin
G_P_ _ _ _	Gravida (# pregnancies) Para (Prior pregnancies-Term, Preterm, Abortions, Alive)
GA	Gestational age
GBS	Group B Streptococcus
GC or G/C	Gonorrhea/Chlamydia
GCT	Glucose Challenge Test
GDM	Gestational diabetes mellitus
GODM	Gestational onset diabetes mellitus
GTT	Glucose Tolerance Test
GU	Genitourinary
HAV	Hepatitis A Virus
HBIG	Hepatitis B Immune Globulin
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCG	Human chorionic gonadotropin
HCV	Hepatitis C virus
HELLP	Hemolysis, elevated liver enzymes, low platelets
HIE	Hypoxemic ischemic encephalopathy
HIV	Human immunodeficiency virus
HLHS	Hypoplastic left heart syndrome
HMD	Hyaline Membrane disease
HPV	Human papillomavirus
HSV	Herpes Simplex Virus

HTLV-1	Human T-cell lymphotrophic virus type I
IDDM	Infant of a drug dependent mother
Inc AB	Incomplete abortion
IUCP	Intrauterine contraceptive device
IUD	Intrauterine device
IUFD	Intrauterine fetal demise
IUGR	Intrauterine growth retardation(restriction)
IUP	Intrauterine pregnancy
IUPF	Intrauterine pregnancy
IUTP	Intrauterine term pregnancy
IVH	Intraventricular hemorrhage
K-B	Kleihauer-Betcke
KOH	Potassium Hydroxide
L/S	Lecithin-to-sphinphomyelin ratio
LAVH	Laparoscopic assisted vaginal hysterectomy
LBW	Low birth weight
LGA	Large for gestational age
LMP	Last menstrual period
LSCS	Lower segment c-section
LSO	Left Salpingo-oophorectomy
LTCS	Lower transverse Cesarean section
Mec	Meconium
MMR	Measles, mumps, rubella
MPC	Mucopurulent cervicitis
NB	Newborn
NBS	New Ballard Score
NEC	Necrotizing enterocolitis
NGU	Nongonococcal urethritis
NRFHT	Non-reassuring fetal heart tones
NST	Non stress test
NSVD	Normal Spontaneous vaginal delivery
NTD	Neural tube defect
OCP	Oral contraceptive pill
OCT	Oxytocin Challenge Test
PAP	Papanicolaou smear
PAT	Pregnancy at term
PDA	Patent ductus arteriosus
PGE1	Alprostadil
PHH	Posthemorrhagic hydrocephalus
PID	Pelvic inflammatory disease
PIE	Pulmonary interstitial emphysema
PIH	Pregnancy induced hypertension
PKU	Phenylketouria
PMP	Previous menstrual period
PMS	Premenstrual syndrome

PNC	Prenatal care
PNV	Prenatal vitamin
PObHx	Past obstetrical history
PPHN	Persistent pulmonary hypertension of newborn
PPROM	Preterm premature rupture of membranes
PPTL	Post partum tubal ligation
PTL	Preterm labor
PVL	Periventricual leukomalacia
RDS	Respiratory Distress Syndrome
Rh	Rhesus blood factor
ROP	Retinopathy of prematurity
RPR	Rapid plasma reagent
RSV	Respiratory Syncytial virus
RVH	Right ventricular hypertrophy
SAB	Spontaneous abortion
SGA	Small for gestational age
SIDS	Sudden infant death syndrome
SPT	Septic Pelvic Thrombosis
SROM	Spontaneous rupture of membranes
STD	Sexually transmitted disease
SVD	Spontaneous vaginal delivery
TAB	Therapeutic Abortion
TAH	Total abdominal hysterectomy
TBLC	Term birth living child
TCA	Trichloroacetic acid
TDx FLM	Tdx fetal lung maturity
THAM	Tromethamine
TOA	Tubo-ovarian abscess
TOF	Tetrology of Fallot
TORCH	Toxoplasmosis, Other (Syphilis Hep B, coxsackie virus, Epstein-Barr, varicella-zoster, human parvovirus, Rubella, Cytomegalovirus, Herpes Simplex
TTN	Transient tachypnea of newborn
TVH	Total vaginal hysterectomy
UAC	Umbilical artery catheter
UC	Uterine contractions
US	Ultrasound
UVC	Umbilical venous catheter
VBAC	Vaginal birth after cesarean section
VI	Vaginal irritation
VIP	Voluntary interruption of pregnancy
VSD	Ventricular septal defect
VTX	Vertex
Vx	Vertex presentation
ZDV	Zidovudine

Prepared by Mirjana Lulic-Botica RPh, Neonatal Clinical Specialist 3/04

Drugs in Pregnancy and Lactation

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(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

Drug risk category changes of pregnancy trimesters

- Examples if this include:
  - ACE inhibitors:
    - No effect in the first trimester but my 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.

Criticisms of current drug risk categories

- 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

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

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.

Lactation Risk Categories

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

Lactation Risk Categories

- 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.

Lactation Risk Categories

- 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.

Guidelines for selecting drugs in the nursing mother

- Determine Relative Infant Dose (RID)
  - RID = Infant dose (mg/kg/day) divided by the Maternal dose (mg/kg/day)
  - A Relative infant dose of <10% is gene rally considered safe

Drugs Contraindicated during breastfeeding

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

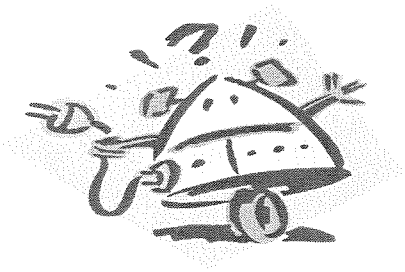
Drugs Contraindicated during Breastfeeding

- 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.

EMERGENCY MEDICATION BOX IN MATERNAL SPECIAL CARE
DOSING GUIDELINES

(last updated 05/04 by M. Lulic-Botica, Neonatal Clinical Specialist)

Drug	Preparation	Dosing Regimen	Maximum Dose / Rate/Comments
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	1st line agent for acute severe hypertension in preeclampsia Rapid IVP over 1-2 minutes Do not exceed 0.2mg/kg/min
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

EMERGENCY MEDICATION BOX IN MATERNAL SPECIAL CARE
CONTENT AND QUANTITIES

Drug	Strength	Quantity	Expiration
Calcium Gluconate	1gram/10ml (100mg/ml)	1	
Furosemide (Lasix®)	10mg/ml 4ml	5	
Hydralazine (Apresoline®)	20mg/ml 1ml	5	
Labetalol (Normodyne®, Trandate®)	5mg/ml 20ml	2	
Methylergonovine (Methergine®)	0.2mg/ml 1ml	2	
Metoprolol (Lopressor®)	5mg/5ml 5ml	4	
Oxytocin (Pitocin®)	10 Units/ml 1ml	2	

Review of OB/GYN population

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Hutzel Women's Hospital
(last updated 12/29/0 4)

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:
    - IUP at 38 4/7 wk GA based on LMP/US
    - C-sect 2 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

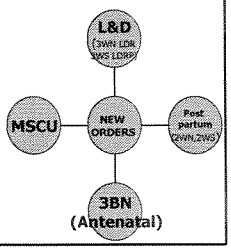
- MSCU (location 3WS) is a maternal ICU. Patient may be pregnant or post-partum.
- OBRR (location 3WS) Sometimes post-op antibiotics are started here especially if post-partum floors are full. Has no tube. Must tube to the MSCU tube station.
- 3WS-OR has C-section OR suites.
- 3WS is LDRP (labor, delivery, 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&) (Admission & Observation nursery)
- SCN – Special Care Nursery (formerly PCN) (2BC)
- NICU – Neonatal Intensive Care Unit (3BC)

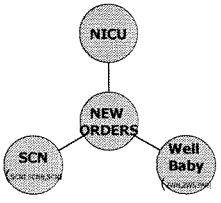
Transfer orders – Adults

- 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 (SCNI, 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

- 1. Refer to 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- 32wks),Vd=0.35 L/kg
- 3rd trimester (33wks 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 the OB/GYN population

- 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 ABX 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 dictate the support of the dose or the need to change it.
- Round doses to nearest 20 mg even increments for gent/tobra.

Pharmacokinetics in OB/GYN population

- <u>High-Peak ODA Goals for Levels:</u>
- 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 the OB/GYN population

- 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

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

Pharmacokinetics in OB/GYN population

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

Pharmacokinetics in OB/GYN population

- 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 urknown in patients with severe penicillin allergy; MUST be discontinuedafter delivery.
    - Std dose: Vancomycin 1 G IVPB q12 untildelivery

Vancomycin documentation

- Documenting use of Criteria-Monitored Antimicrobials
  - Vancomycin
    - P9 (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.

Anticoagulation in the pregnant patient

- Four potential approaches
  - Warfarin throughout pregnancy (widely used in Europe but NOT in the US)
  - Adjust – dose SC UFH throughout pregnancy
    - Maintain mid-interval aPTT > 2x normal
  - LMWH use throughout pregnancy
    - Maintain a 4h post-dose anti-Xa level approx. 1.0 unit/ml
  - UFH or LMWH until the 13th week, change to warfarin until the middle of the 3rd trimester, then restart UFH/LMWH until delivery.
  - No definitive recommendation due to insufficient clinical data: Chest 2001;119(1):122S-131S

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

LMWH use in pregnant women with prosthetic heart valve

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

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
    - Unconjuated 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 that predates pregnancy
    - 2) Preeclampsia-Eclampsia – elevated BP + proteinuria
    - 3) Chronic hypertension with superimposed 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 Angiontensin 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:**
- Ampicillin 2g IVPB q6hr
- Gentamicin 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 >or= 105 mg/dl
    - 1hr >or=190mg/dl
    - 2hr >or=160mg/dl
    - 3hr >or=145mg/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

CLASS	DESCRIPTION
A	Chemical diabetes with a (+) GTT before/during pregnancy
B	Onset after age 20; 10years duration
C	Onset at age 10-19
D1	Onset before age 10
D2	Duration >20 years
D3	Calcification of vessels of the leg
D4	Benign retinopathy
D5	Hypertension
E	Calcification of pelvic vessels
F	Nephropathy
G	Pregnancy failures
H	Vascular lesion devel oping in childbearing years inc. cardiopath y
R	Malignant retinopathy

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 <95-105mg/dl
    - Postprandial goal of <140mg/dl

Gestational Diabetes

- Treatment:
  - 1) Diet controlled
    - Monitoring of glucose levels at least 4 t imes 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)

Gestational Diabetes

- There are some small studies which support the use of very short acting insulin lispro with once-daily extended insulin ultralente
- The use of oral hypoglycemics has not been routinely recommended due to potential risks of teratogenicity and transport of glucose across the placental causing prolonged neonatal hypoglycemia

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 preecla mpsia

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 con trol
    - Blood products transfusion as required
    - Corticosteroid thera py
    - Plasmapheresis for refractory HELLP sy ndrome

HELLP

- Pathogenesis of HELLP is not well understood
  - Multisystem disease attribut ed to abnormal vascular tone, vasospasm and coa gulation defects
  - Syndrome seems to be the final manife station of some insult that lea ds to microvascular endot helial 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

HELLP

- Treatment
  - Antihypertensives:
    - Hydralazine 2.5-5mg IV and titrate
    - Labetalol
    - 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-17ß
  - 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
  - Intravenous fluids
    - Bolus of 500ml of LR/DRLR
    - Rapid intravascular expansion can diminish the contractions
  - Tocolytics
    - Terbutaline 0.25mg SC q1-6hr
    - Magnesium 6g LD then 2-4g/hr
    - Indomethacin 50-100mg po x1 then 25mg q4-hr x48hr
    - Nifedipine 10mg po q8hr maint/30mg XL po qd

Premature labor

- Management
  - Corticosteroids
    - Only treatment shown to improve fetal survival
      - BMC 12mg IM q12 x2 doses OR
      - [illegible]asone 6mg IV q12 x4 doses
  - A[illegible]rythromycin/Clindamycin
  - Emerging Treatments
    - Oxytocin inhibitors
      - Antocin
      - Nonpeptidyl 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 be labor progress
  - Maternal:
    - Labor is weak/erratic/stalled
  - Fetal:
    - Fetal compromise
- Controls 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

- **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
- Titrate to response:
- Contraction duration of 40-60 seconds
- Uterine palpitations indicate strong contraction
- Intrauterine Pressure Catheter shows and 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

Commonly used medications in OB/GYN

- Rate of Drip standard bag of 10 units of Oxytocin/1000ml of IV fluid:
- 10gtts = 1 ml
- 0.5 mu/min = ½ gtt/min = 3ml/hr
- 1 mu/min = 1 gtt/min = 6ml/hr
- 2 mu/min = 2 gtt/min = 12ml/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 = 3ml/hr
- 2 mu/min = 6 ml/hr
- etc.

Commonly used medications in OB/GYN

- **Postpartum bleeding:**
- 10 Units Oxytocin IM after delivery
- 10-40 Units Oxytocin/1000ml of IV fluid given IV

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 population

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

Commonly used medications in OB/GYN population

- **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 antibodes 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

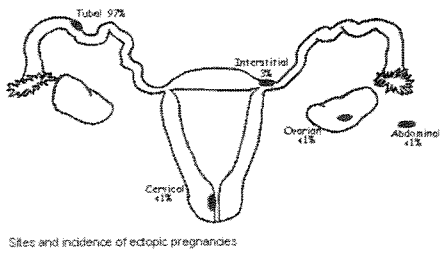
Commonly used medications in OB/GYN populations

- **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

Commonly used medications in OB/GYN population

- **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

Commonly used medications in OB/GYN population



Sites and incidence of ectopic pregnancies

Commonly used medications in the OB/GYN population

- **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)
- PLUS
- Leucovorin 0.1mg/kg PO/IM qod x4 doses on alternating days (Day 2,4,6,8) (Folinic acid)
- (Leucovorin acts as a folic 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- 32wks),Vd=0.35 L/kg
3rd trimester (33wks 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.

■<u>High-Peak ODA Goals for Levels:</u>

- ■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.

12/18/04

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.

HUTZEL WOMEN'S HOSPITAL
REVIEW OF MEDICATIONS IN THE OB/GYN POPULATION

Marianne Lulic-Botica
Clinical Pharmacy Specialist
(last upated 11/04)

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
    - Baseline
    - Variability
    - Periodic/Non-periodic changes
    - Reassuring/Non-reassuring characteristics:
        - Repetitive late heart rate decelerations
        - Repetitive significant variable decelerations (FHR < 70BPM lasting 60 seconds)
        - Prolonged FHR decelerations (FHR <80BPM lasting >90 seconds)
        - Fetal tachycardia (>160 BPM for > 10min)

Maternal:

- Baseline vital signs, BP
- Monitor I/O
- Uterine Activity
    - Contraction pattern
    - Resting tonus
    - Frequency
    - Duration
    - Intensity
- Observe for uterine hyperstimulation
    - > 6 contractions in 10 min x2
    - 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

Dose (mu/min)	Drops/min	Rate/hr
0.5	½	3ml/hr
1	1	6ml/hr
2	2	12ml/hr
3	3	18ml/hr
4	4	24ml/hr
5	5	30ml/hr
6	6	36ml/hr
7	7	42ml/hr
8	8	48ml/hr
9	9	54ml/hr
10	10	60ml/hr

Rate of Drip of standard bag of 10 units of Oxytocin/500ml of IV fluid

Dose (mu/min)	Drops/min	Rate/hr
0.5	½	1.5ml/hr
1	1	3ml/hr
2	2	6ml/hr
3	3	9ml/hr
4	4	12ml/hr
5	5	15ml/hr
6	6	18ml/hr
7	7	21ml/hr
8	8	24ml/hr
9	9	27ml/hr
10	10	30ml/hr

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

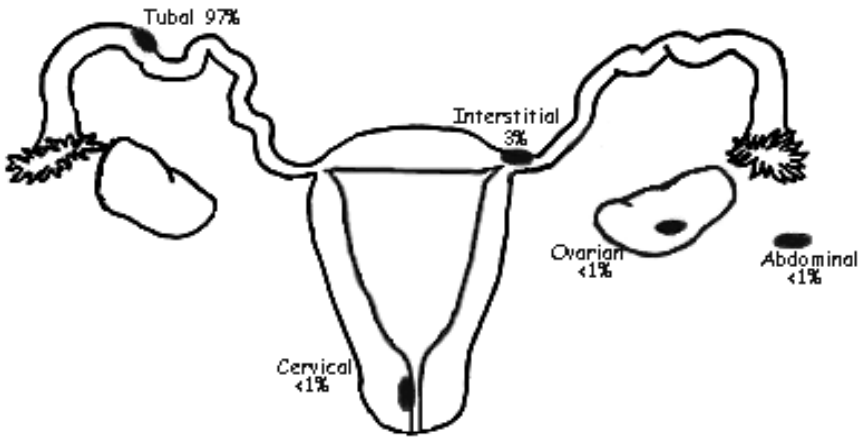
Methotrexate

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

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 x4 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:

$$\text{BSA (m2)} = \frac{\text{Ht (inches)} \times \text{Wt (lbs)}}{3131}$$

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.