Prescribing In Pregnancy and Lactation

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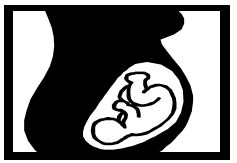

TABLE OF CONTENTS

PREGNANCY RISK FACTOR CLASSIFICATIONS[1, 2]

In addition to the brief overview of the literature concerning each drug and its use in pregnancy and lactation, each drug is assigned a pregnancy risk factor letter of classification. The drug is classified as being in one of 5 categories of risk (A, B, C, D or X) based on the level of risk the drug poses to the fetus. The definitions used for the risk factors are listed below.

A. **SAFE - Controlled studies in pregnant women fail to demonstrate a risk to the fetus in the first trimester with no evidence of risk in later trimesters. The possibility of fetal harm appears remote.**
B. **LIKELY SAFE - Either animal-reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women, or animal-reproduction studies have shown an adverse effects (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester and there is no evidence of a risk in later trimesters.**
C. **CAUTION - Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal effects or other) and there are no controlled studies in women, or studies in women and animals are not available. Drugs should be given only if the potential benefits justify the potential risk to the fetus.**
D. **EXTREME CAUTION - There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g. if the drug is needed in a life threatening situation of for a serious disease for which safer drugs cannot be used or are ineffective)**
X. **CONTRAINDICATED - Studies in animals or humans have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience, or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.**

1. Briggs GG, Freeman RK, Yaffe SJ. Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk -5th Ed. Williams and Wilkins; 1998.
2. Lacy CF, Armstrong LL, Morton GP et al. Drug Information Handbook -11th Ed. Lexi-Comp Inc; 2003.
3. Rx Files – Drug Comparison Chart. Saskatoon Health Region; 2003.

ANTI-INFECTIVES

ANTIBIOTICS

* ***Penicillins, cephalosporins and erythromycin*** **are considered the antibiotics of choice during pregnancy, with wide safe margin[1]**
* ***Aminoglycosides, sulfonamides and metronidazole*** **are NOT CI during pregnancy and can be used when indicated[1]**
* ***Quinolones*** **are not considered teratogenic but are blamed for causing arthropathy in children[1]**
* ***Tetracyclines*** **are not teratogenic but *should be avoided* during 2nd and 3rd trimester due to effects on teeth and bone[1]**
* ***Penicillins and cephalosporins*** **are considered to be safe to use while breast feeding – infants should be observed for allergic reactions[2]**

	Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
AMINOGLYCOSIDES	**Amikacin** AMIKIN **Gentamicin** GARAMYCIN **Neomycin** **Streptomycin* (D)** **Tobramycin** NEBCIN	C	Ototoxicity has not been reported as an effect of in *utero* exposure No reports liking these drugs with congenital defects[3] *Streptomycin: case reports describing ototoxicity in infants whose pregnant mothers were treated with streptomycin Incidence still considered low Incidence of congenital defects same as in healthy control group[3]	Compatible with breast feeding with careful monitoring 3 potential problems for nursing infant: modification of bowel flora, direct effects on infant and interference with the interpretation of culture results if a fever workup is required[3]

* a potentially serious drug interaction may occur in newborns treated with aminoglycosides who were also exposed in *utero* to magnesium sulfate[3]

ANAEROBIC	**Metronidazole** FLAGYL	B	Use in pregnancy is controversial Considered contraindicated during the 1st trimester in patients with trichomoniasis For other indications the risk, benefit ratio must be carefully weighed before its use, especially in 1st trimester[3]	Enters breast milk Not recommended If single dose is given recommend delay breast feeding for 12 hrs[4]

	Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
CEPHALOSPORINS	1st **Cefazolin** **ANCEF, KEFZOL** **Cephalexin** **KEFLEX** 2nd **Cefotetan** **CEFOTAN** **Cefprozil** **CEFZIL** **Cefuroxime** **CEFTIN** 3rd **Cefixime** **SUPRAX** **Ceftriaxone** **ROCEPHIN** 4th **Cefepime** **MAXIPIME**	B	Usually considered safe during pregnancy[3] One of the antibiotics of choice during pregnancy[1]	Compatible[3]
MACROLIDES	**Azithromycin** **ZITHROMAX**	B	Limited human studies Single dose treatment for chlamydial infections not recommended during pregnancy or lactation – safety and efficacy have not been established[3]	Accumulated in breast milk due to its lipid solubility and ion trapping of a weak base[3]
	Clarithromycin **BIAXIN**	C	No published reports describing its use during human pregnancy Case reports of use and congentital malformations – may or may not be due to chance[3]	Risk is probably minimal, but because it is a new drug, caution should be exercised[3]

	Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
MACROLIDES CONT.	**Erythromycin** **ERYC, PCE**	**B**	No reports linking its use with congenital defects have been located[3] Considered an antibiotic of choice during pregnancy[1]	Compatible[3]

OTHER	**Nitrofurantoin** **MACRODANTIN, MACRIBID**	**B**	No association with congenital defects Studies support the safety of its use in pregnancy Manufacturer package insert carries a warning against its use at term due to risk of hemolytic anemia in newborns due to already decreased levels of glutathione in fetal RBC's[3]	Compatible[3]
	Polymyxin B	**B**	No association with congenital defects has been observed[3]	No data available[3]
	Rifampin **RIFADIN, ROFACT**	**C**	No controlled studies have linked its use with congenital defects Has been implicated as one of the agents responsible for hemorrhagic disease of the newborn – prophylactic Vit K_1 is recommended to prevent this[3]	Compatible[3]
	Trimethoprim **PROLOPRIM**	**C**	Caution has been advocated for use in pregnancy due to its folate antagonist properties Published case reports and placebo controlled trials have failed to demonstrate an increase in fetal abnormalities, however some unpublished data are suggestive of an association between the drug combo trimethoprim-sulfamethoxazole and its use in the 1st trimester with congenital defects[3]	Compatible[3]

	Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
OTHER CONT.	**Vancomycin** **VANCOCIN**	C	No cases of congenital defects attributable to vancomycin have been reported[3]	Poorly absorbed form GI tract, thus systemic absorption not expected However, 3 potential problems exist for nursing infant: modification of bowel flora, direct effects on infant and interference with the interpretation of culture results if a fever workup is required[3]
PENICILLINS	**Amoxicillin** **AMOXIL** **Ampicillin** **Cloxacillin** **Penicillin V** **PEN-VEE**	B	Considered one of the antibiotics of choice during pregnancy due to wide safety margin[1] No reports linking penicillins with congenital defects[3]	3 potential problems exist for nursing infant: modification of bowel flora, direct effects on infant (e.g. allergic response or sensitization) and interference with the interpretation of culture results if a fever workup is required[3]
FLUOROQUINOLONES	**Ciprofloxacin** **CIPRO** **Levofloxacin** **LEVAQUIN** **Norfloxin** **NOROXIN**	C	Use during gestation does not appear to be associated with an increased risk of major congenital malformations, however, a causal relationship with some of the birth defects cannot be excluded Because of this and the available animal data, its use, especially during 1st trimester should be considered contraindicated, especially since there are safer agents available[3]	Not recommended because of the potential for arthropathy (based on animal data) and other serious toxicity in the nursing infant[3]

	Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
TETRACYCLINES	**Doxycycline** **VIBRAMYCIN** **Minocycline** **MINOCIN** **Tetracycline**	**D**	Problems can be classified into 4 areas: 1. Adverse effects on fetal teeth and bones[3] (yellow, gray-brown, or brown staining of deciduous teeth; destruction of enamel) Relative risk: from 4 months of gestation and on occurs in 50% of exposed fetuses: If exposure before 14-16 weeks no known risk[1] 2. Maternal liver toxicity[3] 3. Congenital defects[3] 4. Miscellaneous effects[3]	Considered compatible – theoretically, dental staining and inhibition of bone growth could occur in breastfed infants[3] 3 potential problems exist for nursing infant: modification of bowel flora, direct effects on infant (e.g. allergic response or sensitization) and interference with the interpretation of culture results if a fever workup is required[3]
TOPICAL	**Bacitracin** **BACIGUENT** **Neomycin**	**C**	No reports linking use with congenital defects[3]	No data[3]

ANTIFUNGALS

*** Few of the antifungals have been proven to be teratogenic in animal studies (in human studies, only systemic *griseofulvin* has been associated with congenital malformations)**
*** Any topical antifungal can be used during pregnancy**
*** Vaginal application should be avoided after the amniotic membranes have ruptured[2]**

Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
Amphotericin B **FUNGIZONE**	**B**	No evidence of adverse fetal effects Can be used in pregnancy in those who will clearly benefit[3]	No data[3]
Clotrimazole **CANESTEN**	**B**	Has been used topically in pregnancy and no associations with congenital malformations have been reported[2]	No data[3]
Fluconazole **DIFLUCAN**	**C**	Limited data suggests use during 1st trimester to be teratogenic with continual daily doses of 400mg/d or more Safety of lower doses has not been established but risks for adverse effects appear low, especially after short, low dose courses for vaginal fungal infections[3]	Probably safe[3]
Griseofulvin **FULVICIN**	**C**	Systemic therapy associated with congenital malformations[2] Because the use of an antifungal agent is seldom essential during pregnancy its use should be avoided at this time[3]	No data[3]
Itraconazole **SPORANOX**	**C**	Available human data are too limited to determine whether it possess a risk to the fetus for congenital anomalies Should be avoided during organogenesis until further data are available see fluconazole[3]	Potential effects of exposure have not been studied Advise against use[3]

* Antifungals may be capable of inducing human malformations[3]

ANTIFUNGALS CONT…..

Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
Ketoconazole **NIZORAL**	C	Some case reports of fetal limb defects[3]	No data[3]
Miconazole **MICATIN, MICOZOLE, MONISTAT**	C	Has been associated with an increase in fetal mortality in different animal studies when administered during active organogenesis No reports of fetal adverse effects in humans[2]	No data[3]
Nystatin **NILSTAT, CANDISTATIN, MYCOSTATIN**	B	Poorly absorbed and its use has not been associated with teratogenesis[2] Data do not support an association between the drug and congenital defects[3]	Because the drug is poorly absorbed, if at all, serum and milk levels would not occur[3]
Terbinafine **LAMISIL**	B	Avoid use in pregnancy since treatment of onychomycosis can be postponed[4]	Excreted in breast milk Not recommended[4]

ANTIVIRALS

Acyclovir **AVIRAX, ZOVIRAX**	C	No adverse effects in the fetus or newborn attributable to its use during pregnancy have been reported Risks appear minimal, but insufficient data at present to establish safety of use during pregnancy Long term studies are needed[3]	Compatible[3]
Amantadine **SYMMETREL**	C	Embryotoxic and teratogenic in animals in higher doses Infrequent use in pregnant women therefore data is lacking Theoretically may be a human teratogen[3]	Use with caution because of potential for urinary retention, vomiting and skin rash No reports of adverse effects in nursing infants[3]

ANTIVIRALS CONT…..

Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
Famciclovir **FAMVIR**	**B**	No reports describing use during human pregnancy No embryonic or teratogenic effects observed in animal studies Tumorogenicity observed in rats[3]	Should not breast feed while taking[3]

REFERENCES:

1. Motherisk Program at the Hospital for Sick Children [Internet homepage]. Toronto, Canada: c 2001 [cited 2005 Jan 11]. Available from http://www.motherisk.org
2. Koren G. Maternal-Fetal Toxicology: A Clinician's Guide -2nd Ed. Marcel Dekker Inc; 1994.
3. Briggs GG, Freeman RK, Yaffe SJ. Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk -5th Ed. Williams and Wilkins; 1998.
4. Lacy CF, Armstrong LL, Morton GP et al. Drug Information Handbook -11th Ed. Lexi-Comp Inc; 2003.

ASTHMA PHARMACOTHERAPY

*** None of the medications used for the treatment of acute asthmatic attacks has been incriminated as a teratogen[1]**
*** The current approach is to treat optimally asthmatic attacks during pregnancy, since the complications of untreated asthma far outweigh unproven reproductive effects associated with the medications[1]**

	Generic/ TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
CORTICOSTEROIDS (INHALED)	**Beclomethasone diproprionate (BDP)** QVAR **Budesonide (C/B)** PULMICORT **Fluticasone** FLOVENT	C	Epidemiologic data on inhaled corticosteroids have shown no increase in rates of congenital malformations Currently recommended as part of routine management of moderate to severe chronic asthma during pregnancy[2]	Other corticosteroids are excreted into breast milk in low concentrations Use with caution[3]
LABA (INHALED)	**Formoterol** OXEZE **Salmeterol** SEREVENT	C	No adequate well controlled studies in pregnancy Use if benefit to mother outweighs potential risk to fetus[4]	Limited data Use with caution[4]
SABA (INHALED)	**Fenoterol** **Salbutamol (C)** VENTOLIN **Terbutaline**	B	No reports linking use of Fenoterol with congenital defects[3] No human studies on the 1st trimester use of salbutamol. May cause fetal tachycardia and maternal hyperglycemia[1] No published reports found regarding use in pregnant asthmatic patients[3]	Terbutaline considered compatible with breast feeding No data on Fenoterol or Salbutamol[3]

*** The use of inhaled beta-adrenergic agonists during pregnancy does not cause any significant increase in incidences in fetal defects or labor complications[1]**

	Generic/ TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
OTHER	**Ipatropium** **ATROVENT** **(anticholinergic agent)**	**B**	Human data rare No evidence that the drug is hazardous to the fetus[3]	Limited data Amounts excreted into breast milk after inhalation are probably insignificant[3]
	Theophylline **(bronchodilator)**	**C**	Has not been associated with an increased teratogenic risk or still births in humans[1] Bronchodilator of choice for asthma and chronic obstructive pulmonary disease in the pregnant patient[3]	Compatible[3]

REFERENCES

1. Koren G. Maternal-Fetal Toxicology: A Clinician's Guide -2nd Ed. Marcel Dekker Inc; 1994.
2. Motherisk Program at the Hospital for Sick Children [Internet homepage]. Toronto, Canada: c 2001 [cited 2005 Jan 11]. Available from http://www.motherisk.org
3. Briggs GG, Freeman RK, Yaffe SJ. Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk -5th Ed. Williams and Wilkins; 1998.
4. Lacy CF, Armstrong LL, Morton GP et al. Drug Information Handbook -11th Ed. Lexi-Comp Inc; 2003.

CARDIOVASCULAR

ANTIHYPERTENSIVES

*** Exposure during 2nd and 3rd trimesters of pregnancy to ACE Inhibitors is associated with development of kidney failure in the fetus, leading to intrauterine growth retardation, oligohydramnios and hypoplasia of skull bones[1]**
*** 1st trimester exposure has not been associated with increased risk of structural malformations[1]**
*** *Therefore, ACEI's are considered CI during 2nd and 3rd trimesters*, but 1st trimester exposure should not be an indication for termination[1]**

	Generic/ TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
ACE INHIBOTORS	**Captopril** **CAPOTEN** **Enalapril** **VASOTEC** **Fosinopril** **MONOPRIL** **Lisinopril** **ZESTRIL,** **PRINIVIL** **Perindopril** **COVERSYL** **Quinapril** **ACCUPRIL** **Ramapril** **ALTACE**	**D**	Present a major risk to the fetus in terms of toxicity, including: • fetal and neonatal renal failure • intrauterine growth retardation • prematurity • severe neonatal hypotension • fetal and neonatal death • oligohydramnios • pulmonary hypoplasia • limb contracture • craniofacial deformation Appear to be teratogenic in 2nd and 3rd trimesters causing fetal calvarial hypoplasia and renal anomalies The cause of these defects is probably related to fetal hypotension and decreased renal blood flow[2]	Considered compatible but limited data Use with caution[2]

*** Unclear whether benefits outweigh risks when beta-blockers are used to treat mild to moderate chronic or pregnancy-induced hypertension, given the unknown overall effect on perinatal outcomes[3]**
*** Reports of fetal growth retardation, bradycardia, and hypoglycemia associated with their use during gestation have been published[1]**
*** Most neonates have not shown any adverse clinical signs; fetuses exposed in *utero* to beta-blockers should be closely monitored with serial ultrasounds and neonates should be followed for potential bradycardia or hypoglycemia[1]**

BETA-BLOCKERS

Generic/ TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
Atenolol **TENORMIN** **(beta$_1$- selective)**	**D**	In *utero* exposure may result in intrauterine growth retardation Infant behavior not affected[2]	Nursing infant must be closely monitored for bradycardia and other signs and symptoms of β-blockade Long term effects not studied; consider safer alternatives i.e.propranolol[2]
Labatalol **TRANDATE** **(beta and alpha$_1$ adrenergic blocker)**	**C**★ **(*D if used in 2nd or 3rd trimester)**	Does not seem to pose a risk to fetus except possibly in 1st trimester May offer advantage over the use of agents with only beta-blocker activity Growth retardation not a concern Benefits in some cases may outweigh risks[2]	Long term effects of exposure have not been studied Considered compatible[2]
Metoprolol **LOPRESSOR** **(beta$_1$-selective)**	**C**★ **(*D if used in 2nd or 3rd trimester)**	Has been used during pregnancy for the treatment of maternal hypertension and tachycardia No fetal malformations attributed to the drug have been reported but experience during the 1st trimester is limited[2]	Milk concentrations are ~3x those found simultaneously in maternal serum Drug is considered compatible with breast feeding with appropriate infant monitoring[2]
Propranolol **INDERAL** **(non-selective)**	**C**★ **(*D if used in 2nd or 3rd trimester)**	Has been used for various indications in pregnancy Not considered a teratogen but fetal and neonatal toxicity may occur[2]	Compatible Nursing infants should be closely observed for symptoms of beta-blockade[2]

*The benefits of maternal therapy with beta-blockers may, in some cases outweigh the risks to the fetus and must be judged on a case by case basis[2]

	Generic/ TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
CALCIUM CHANNEL BLOCKERS	**Amlodipine** **NORVASC**	C	No reports of use in human pregnancy found[2]	No data available[2]
	Nifedipine **ADALAT**	C	Use during pregnancy is controversial Should be reserved for women with severe hypertension who are unresponsive to standard therapy or in controlled trials until toxicity has been studied more carefully[2]	Compatible[2]
OTHER ANTIHYPERTENSIVES	**Hydrazaline** **APRESOLINE**	C	No reports linking drug with congenital defects Most commonly used antihypertensive therapy in England[2] For severe 'late-onset' pregnancy hypertension IV Labatolol is safer than IV Hydrazaline or Diazoxide[3]	Compatible[2]
	Methyldopa **ALDOMET**	C	Regarded by many as a **drug of choice** for managing hypertension during pregnancy, mainly because of its safety profile[2]	

ANTIPLATELET/ ANTITHROMBOTIC AGENTS

	Generic/ TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
ORAL AGENTS	**Aspirin/ASA** **ENTROPHEN**	**C*** **(*D if full dose aspirin used in 3rd trimester)**	Chronic or intermittent high doses should be avoided[2] No fetal or neonatal toxicity was observed after chronic use of low dose aspirin[1]	Should be used cautiously by the mother during lactation because of potential adverse effects in the nursing infant[2]
	Warfarin **COUMADIN**	**D**	Known teratogen[4] Avoid in 1st trimester as significant risk to fetus exists Avoid exposure in 6th-9th weeks of gestation- produces a patterns of defects termed Fetal Warfarin Syndrome (FWS) Avoid use at term[2]	Compatible[2]
INJECTABLE AGENTS	**Dalteparin** **FRAGMIN**	**B**	Not expected to cross placenta due to high molecular weight Appears to present no more fetal or newborn risk, and perhaps less, than that from standard, unfractionated heparin or from on therapy[2]	Risk appears to be negligible Drug would be inactivated in GI tract[2]
	Heparin **HEPALEAN**	**B**	Has not been related to congenital defects nor does it cross the placenta Appears to have major advantages over oral anticoagulants as the treatment of choice during pregnancy Long term treatment during pregnancy has been associated with maternal osteopenia[2]	Is not excreted into breast milk because of its high molecular weight[2]

LIPID LOWERING THERAPY

*** Current recommendations suggest *discontinuing statin medications* before conception, especially since stopping therapy for the relatively short duration of pregnancy is believed to have little effect on long term outcome. However, with new evidence that suggests maternal hypercholesterolemia has a detrimental effect on the developing fetus, this recommendation might change[1]**

STATINS\HMG

Generic/TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
Atorvastatin **LIPITOR** **Fluvastatin** **LESCOL** **Lovastatin** **MEVACOR** **Pravastatin** **PRAVACHOL** **Rosuvastatin** **CRESTOR** **Simvastatin** **ZOCOR**	**X**	Limited information therefore should be avoided in pregnancy[5] Interruption of therapy to have no long term effects on treatment of hyperlipidemia; use is CI[5,2]	CI in pregnancy[5] Potential for adverse effects in nursing infant[2]

RESINS

FIBRATES

Generic/TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
Cholestyramine **QUESTRAN**	**B**	Has been used for the treatment of cholestasis in pregnancy Only one case of adverse fetal effects[2]	No reports of use Binds to fat soluble vitamins therefore prolonged use may result in deficiencies in mother and nursing infant[2]
Gemfibrozil **LOPID**	**C**	Effects in pregnant women not well studied Should only be used during pregnancy if potential benefit justifies potential risk to fetus[2]	Not known whether or not its secreted in human milk Has been shown to produce tumors in animal studies[2]

*note – women with hypertriglyceridemia are prone to gestational pancreatitis, a condition carrying substantial maternal and fetal risk[6]

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1. Motherisk Program at the Hospital for Sick Children [Internet homepage]. Toronto, Canada: c 2001 [cited 2005 Jan 11]. Available from http://www.motherisk.org
2. Briggs GG, Freeman RK, Yaffe SJ. Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk -5th Ed. Williams and Wilkins; 1998.
3. Magee LA, Elran E, Bull SB. Risks and Benefits of Beta-receptor Blockers for Pregnancy Hypertension: Overview of the Randomized Trials. EJOGRB 2000; 88(1): 15-26
4. Koren G. Maternal-Fetal Toxicology: A Clinician's Guide -2nd Ed. Marcel Dekker Inc; 1994.
5. Drugs.com Drug Information Online [Internet homepage]. Micromedex, Inc; c 2005 [cited 2005 Jan 12]. Available from http://www.drugs.com
6. Sanderson SL, Iverius PH, Wilson DE. Successful Hyperlipemic Pregnancy. JAMA 1991; 265:14.

DIABETES

	Generic/ TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
INSULIN	**Insulin**	**B**	**Drug of choice for the control of diabetes mellitus in pregnancy** Animal insulin crosses the human placenta[1]	Does not pass into breast milk[1]
ORAL AGENTS FOR DIABETES	**Glyburide** **DIABETA** **(sulfonylurea/ hypoglycemic agent)**	**C**	If used during pregnancy, therapy should be changed to insulin and glyburide discontinued before delivery to lessen the probability of prolonged hypoglycemia in the newborn[1]	Limited data Hypoglycemia is a potential toxicity[1]
	Metformin **GLUCOPHAGE, GLYCON** **(biguanide)**	**B**	Carefully prescribed insulin therapy will provide better control of the mothers blood glucose, thereby preventing the fetal and neonatal complications that occur with this disease[1]	Effect on nursing infant is unknown[1]

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1. Briggs GG, Freeman RK, Yaffe SJ. Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk -5th Ed. Williams and Wilkins; 1998.

GASTROINTESTINAL

*** Acid-suppressing drugs, mainly H2-blockers and omeprazole, do not appear to cause measurable teratogenic risk in humans[1]**
*** Given the much wider experience with ranitidine than with omeprazole H2-blockers should remain the drugs of choice at present[1]**

	Generic/ TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
H2-RECEPTOR ANTAGONISTS	**Cimetidine** **TAGAMET**	**B**	No congenital malformations in humans have been reported Feminization observed in some animals and non-pregnant humans May consider ranitidine as alternative therapy[2]	Compatible[2]
	Ranitidine **ZANTAC**	**B**	No antiadrogenic activity in humans No problems in newborn attributable to treatment have been reported[2]	Ranitidine decreases gastric acidity, but this effects has not been studied in nursing infants[2]
PROTON PUMP INHIBITORS	**Omeprazole** **LOSEC**	**C**	Unusual patterns of congenital malformations have been reported Until more data are available exposure should be avoided – at least during the 1st half of gestation[2]	Limited data Suppression of gastric acid secretion in infants is a concern Best to avoid[2]
	Rabeprazole **PARIET**	**C**	Not shown to be teratogenic in animal studies Adequate and well-controlled studies have not been done in humans Use only if clearly needed[3]	Excretion in breast milk unknown Not recommended[3]

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1. Motherisk Program at the Hospital for Sick Children [Internet homepage]. Toronto, Canada: c 2001 [cited 2005 Jan 11]. Available from http://www.motherisk.org
2. Briggs GG, Freeman RK, Yaffe SJ. Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk -5th Ed. Williams and Wilkins; 1998.
3. Lacy CF, Armstrong LL, Morton GP et al. Drug Information Handbook -11th Ed. Lexi-Comp Inc; 2003.

PAIN

MIGRAINE – ACUTE TREATMENT

	Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
ERGOTS	**Dihydroergotamine** **MIGRANAL**	X	Considered oxytocic and should not be used during pregnancy[1]	May be excreted in breast milk Contraindicated[1]
	Ergotamine **CAFERGOT**	D	Risk has not been adequately defined Also has oxytocic properties Should be avoided during pregnancy[2]	Ergot alkaloids may hinder lactation by inhibiting maternal pituitary prolactin secretion[2]
TRIPTANS	**Naratriptan** **AMERGE** **Rizatriptan** **MAXALT** **Sumatriptan** **IMITREX** **Zolmitriptan** **ZOMIG**	C	Sumatriptan- Insufficient sample size studied Number of congenital malformations reported with 1st trimester exposure does not appear to be different from a non-exposed population[2] Limited information available on other triptans	Amount of sumatriptan reaching the systemic circulation of a breast feeding infant is probably negligible[2] Others excretion in breast milk is unknown – use with caution[1]

NARCOTIC ANALGESICS

OPIODS

Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
Codeine **CODEINE**	**C*** **(*D if used for prolonged periods or high doses at term)**	Use near term may cause a narcotic withdrawal syndrome in the newborn manifested as tremor, jitteriness, diarrhea and poor feeding[2] During labor, neonatal respiratory depression can occur to the same magnitude as other narcotics[3]	Compatible Passes into breast milk in very small amounts that are probably insignificant[2]
Meperidine **DEMEROL**	**B*** **(*D if used for prolonged periods or high doses at term)**	Problems associated when administered during labor including: Affect on fetal respiratory depression, heart rate, and oxygen consumption Withdrawal symptoms and neonatal addiction are also concerns when used inappropriately [3]	Compatible[2]
Morphine **STATEX, MS-IR, M.O.S.**	**B*** **(*D if used for prolonged periods or high doses at term)**	Chronic use results in neonatal withdrawal Morphine given during labor results in observations of respiratory depression and decreased oxygen consumption[2]	Compatible New data indicate that nursing infants of mothers consuming morphine could be exposed to clinically significant amounts of the narcotic[2]

NSAIDS AND OTHER ANALGESICS

*** NSAIDS not considered teratogenics in animals or humans. Due to their effects on prostaglandins they may cause premature closure of the ductus arteriosus, oligohydroamnion and bleeding complications[3]**
*** Drugs in this class have also been shown to inhibit labor and prolong length of pregnancy[3]**
*** Women attempting to conceive should not use any prostaglandin synthesis inhibitor because of the findings in a variety of animal models that indicate these agents block blastocyst implantation[2]**

	Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
NON-NSAID	**Acetaminophen** **TYLENOL**	**B**	Routinely used during all stages of pregnancy for pain relief and to lower elevated body temperature Apparently safe for short-term use Non-teratogenic in therapeutic doses[3]	Compatible[2]
SALICYL-ATES	**Aspirin/ASA** **ENTROPHEN**	**C★** **(*D if full dose aspirin used in 3rd trimester)**	Chronic or intermittent high doses should be avoided[2] No fetal or neonatal toxicity was observed after chronic use of low dose aspirin[3]	Should be used cautiously by the mother during lactation because of potential adverse effects in the nursing infant[2]
NSAIDs: NON-SELECTIVE COX INHIBITORS	**Diclofenac *(see + Misoprosatal below)** **VOLTAREN** **Ibuprofen** **ADVIL, MOTRIN** **Indomethacin** **INDOCIN, INDOCID** **Ketorolac (*C)** **TORADOL** **Mefenamic Acid (*C)** **PONSTAN** **Meloxicam (*C)** **MOBICOX** **Naproxen** **NAPROSYN**	**B★** **(*D if used in 3rd trimester or near delivery)**	When multiple doses are administered during the later half of pregnancy pharmacologic consequences include: constriction of the ductus arteriosus in *utero*, inhibition of labor, prolongation of pregnancy and suppression of fetal renal function[2] Indomethacin: only studied as a tocolytic agent in pregnancy Other uses should be approached with caution Oliguric renal failure, hemorrhage, and intestinal perforation have been reported in premature infants exposed immediately before delivery[2]	Compatible[2] Mefenamic Acid: usually compatible; other agents in this class may be considered safer agents (diclofenac, ibuprofen, ketorolac)[2]

	Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
NSAIDs: COX 2 SELECTIVE	**Celecoxib** **CELEBREX** **Valdecoxib** **BEXTRA**	**C*** **(*D if used in 3rd trimester or near delivery)**	Use should be avoided in late pregnancy – may cause premature closure of the ductus arteriosus[1]	Excretion in breast milk unknown Not recommended[1]
COMBO PRODUCTS	***Diclofenac and Misoprostol** **ARTHROTEC**	**X**	Contraindicated Misoprostal is an abortifacient Reports of fetal death, congenital anomalies, uterine perforation, and abortion have been received after the use of misoprostal in pregnancy[1]	Excretion in breast milk is unknown Contraindicated[1]

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PSYCHOTROPICS

ANTICONVULSANTS

*** The new anticonvulsants are not recommended in pregnancy and require further research to prove their safety in humans[1]**
*** Proper seizure control is the primary goal in treating women with epilepsy[1]**

Generic/ TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
Carbamazepine **TEGRETOL**	**C**	Crosses placenta Fetal levels are 50-80% of maternal serum levels[2] Association between the drug and congenital defects Increased risk for neural tube defects[3]	Compatible[2]
Gabapentin **NEURONTIN** **Lamotrigine** **LAMICTAL**	**C**	Limited data No conclusion as to whether or not it can be safely used[2]	No data[2] Manufacturer recommends avoidance of use during breast feeding If used infant should be closely Monitored[2]
Phenobarbital **Phenytoin** **DILANTIN** **Valproic acid** **DEPAKENE**	**D**	Therapy presents a risk to the fetus in terms of major and minor congenital abnormalities and hemorrhage at birth The risk to the mother, however, is also great if her seizures are uncontrolled[2]	Major adverse effects in some nursing infants and should only be used with caution[2] Compatible[2]

ANTIDEPRESSANTS

	Generic/TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
SSRI'S	**Fluoxetine** **PROZAC** **Fluvoxamine (C)** **LUVOX** **Paroxetine** **PAXIL** **Sertraline** **ZOLOFT**	**B**	Need for ongoing medication should be evaluated, however changing to another antidepressant is not indicated[4] Limited data does not support a teratogenic risk Potential for behavioral teratogenic effects cannot be exluded Fluoxetine may be preferred agent due to post marketing surveillance data[2]	Are excreted into breast milk Effects to infant unknown but may be of concern[2]
	***There is no substantial evidence that exposure to *tricyclic antidepressants* (TCA's), even in the 1st trimester, carries any significantly increased risk of malformation. However, there is a much higher lethality in overdose when compared with SSRI's[4]**			
TCA'S	**Amitriptyline (D)** **ELAVIL** **Clomipramine** **ANAFRANIL** **Desipramine** **NORPRAMIN** **Doxepin** **SINEQUAN** **Imipramine (D)** **TOFRANIL** **Nortriptyline (D)** **AVENTYL**	**C**	Bulk of evidence indicates safe to use in pregnancy Does not appear to be teratogenic Neonatal toxicity is a concern that appears to be caused by drug withdrawal due to exposure throughout the pregnancy Occasional reports have associated the use of **amitriptyline** use with malformations **Nortriptyline** use has been associated with urinary retention in the neonate as well as reports of limb reduction anomalies which may or may not be directly related to drug use[2]	Effect on nursing unknown (some concern over infants neurobehavioral mechanisms) therefore use with caution[2]

	Generic/TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
OTHER	**Bupropion** **WELLBUTRIN**	**B**	Limited data No birth defects observed in a surveillance study of 3 newborns exposed during 1st trimester[2]	Excreted in breast milk No adverse effects seen in one case report, however, as with all antidepressants, effects on nursing infant is unknown and should be used with caution[2]
	Venlafaxine **EFFEXOR**	**C**	Preliminary data suggest no association with congenital abnormalities[4]	No reports describing its use during lactation Due to its low molecular weight passage into milk should be expected[2]

*The safety during pregnancy of **mirtazapine, moclobemide,** and **nefazodone** has not been adequately studied[4]

ANTIPSYCHOTICS

*** The goal of treatment is to minimize risk of fetal exposure to psychotropic drugs while limiting risks of untreated psychiatric disorder. Ideally the women should be on the *lowest dose possible* to treat her symptoms[5]**

TYPICAL ANTIPSYCHOTICS	**Chlorpromazine** **LARGACTIL** **Haloperidol** **HALDOL**	**C**	Limited data available suggest no serious problems Some evidence relating to chlorpromazine suggests a small increased risk of congenital abnormalities Larger doses, especially if given continuosly, may cause protracted withdrawl dyskinesias in the neonate[4]	Effect on nursing infant unknown Infant may experience drowsiness and lethargy Concern of galacorrhea induced in adults[2]
ATYPICAL ANTIPSYCHOTICS	**Clozapine (B)** **CLOZARIL** **Olanzapine** **ZYPREXA** **Quetiapine** **SEROQUEL** **Risperidone** **RISPERDAL**	**C**	The safety of atypical antipsychotics has yet to be established Case reports and small series reveal no deleterious effects on the fetus When changing a woman from a typical to an atypical antipsychotic warning them about the normalization of fertility is warranted[4] Weight gain caused by atypicals shown to increase risk of neural tube defects in infants of adipose women[6]	Olanzapine enters breast milk – use is CI Excretion of others into breast milk is unknown, therefore not recommended[7] If used monitor baby for any side effects, e.g. drowsiness or floppiness, and ensure lowest dose possible[5]

AXIOLYTICS AND HYPNOTICS

	Generic/TRADE	PREGNANCY RISK FACTOR	FETAL RISK SUMMARY	BREAST FEEDING SUMMARY
BENZODIAZEPINES	**Alprazolam** **XANAX** **Clonazepam (C)** **RIVOTRIL** **Diazepam** **VALIUM** **Lorazepam** **ATIVAN**	**D**	Controversy over whether 1st trimester exposure is associated with increased risk of cleft lip and/or palate Can cause floppy infant syndrome if taken late in pregnancy Neonatal withdrawal symptoms have also been reported[4]	Is excreted into breast milk and may accumulate in infants Effects unknown but may cause lethargy and loss of body weight with chronic use Use not recommended[2]
SEDATIVES	**Zaleplon** **STARNOC** **Zopiclone** **IMOVANE**	**C**	No available data to enable a definitive judgment to be made about the safety of these drugs Evidence form a small series suggests that zopiclone is not a major human teratogen[4] Not recommended for use in pregnancy[7]	Enters breast milk/ not recommended[7]

MOOD STABILIZERS

ANTIMANIC AGENT	**Lithium** **CARBOLITH,** **DURALITH**	**D**	Avoid if possible In mother renal lithium clearance rises during pregnancy[2]	Considered CI[2] If initiated infants behavior and lithium serum levels must be carefully monitored Breast feeding may be continued as long as infants blood levels remain well below therapeutic concentrations and the infant shows no signs of toxicity[8]

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XTRAS

CORTICOSTEROIDS-SYSTEMIC/TOPICAL

*** The use of corticosteroids in animals has been associated with several toxic effects. Fortunately, none of these effects has been observed in human investigations[1]**
*** *Systemic* corticosteroids do not seem to pose a major teratogenic risk for humans; there is a small but statistically significantly increased risk of oral clefts with 1st trimester exposure[2]**
*** Systemic effects of *topical* steroids are generally limited because only 3% of the medication in topical preparations is absorbed following 8 hours of contact with normal skin. However, when used long term or on large areas of skin, they might have systemic effects[3]**

Generic/ TRADE	Pregnancy Risk Factor	Fetal Risk Summary	Breast Feeding Summary
Betamethasone **CELESTODERM, BETNOVATE, TOPISONE**	**C**	No reports of congenital defects with use In children born of mothers treated with drug for premature labor, studies conducted at 4 and 6 years of age have found no difference from controls in cognitive and psycosocial development[1]	No data[1]
Cortisone **CORTONE**	**D**	Some reports of congenital malformations associated with 1st trimester exposure Reports likely reflective of a much greater use of cortisone and not necessarily of a more potent teratogen vs. other glucocorticoids[1]	No data[1]
Dexamethasone **DEXASONE**	**C**	Long term follow-up evaluations of children exposed in *utero* have shown no adverse effects from this exposure[1]	No data[1]
Hydrocortisone **CORTATE**	**C**	Lack of adequate studies in women Use only if potential benefit to mother exceeds the potential risk to fetus Avoid prolonged use or high doses[4]	No data[4]
Prednisone	**B**	Metabolized to prednisolone Appears to have little if any effects on the developing fetus May be increased risk of oral cleft[1]	Compatible[1]

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