

CaseMed-Pregnancy Resource Newsletter

February 2008

MEDICAL STUDIES

Pharmacokinetics studies in pregnant women

Anger GJ, Piquette-Miller M

Clin Pharmacol Ther, 2008; 83(1): 184-7

According to the authors, determining the teratogenicity of new drugs currently dominates the objectives of pregnancy-relevant experiments conducted throughout drug development. This often comes at the expense of valuable pharmacokinetics studies, which are seldom performed pre-market. The purpose of this report is to highlight this issue and illustrate how current methods used to obtain pharmacokinetics data in pregnancy are insufficient. The authors also discuss the steps that are being taken to address this issue.

Early thimerosal exposure and neuropsychological outcomes

Bernard S

N Engl J Med, 2008; 358(1): 93-4; author reply 94

No abstract available.

Betamethasone impairs cerebral blood flow velocities in very premature infants with severe chronic lung disease

Cambonie G, Mesnage R, Milési C, et al

J Pediatr, 2008; 152(2): 270-5

The objective of this study was to assess the effects of betamethasone on the cerebral hemodynamics of neonates with severe chronic lung disease. Results show that betamethasone decreases the cerebral flow velocities of premature infants, suggesting a vasoconstrictor effect in both superficial and deep arterial vessels. Cambonie and colleagues recommend exercising caution when using betamethasone to treat preterm infants with severe chronic lung disease.

Drug safety in pregnant women and their babies: ignorance not bliss

Chambers CD, Polifka JE, Friedman JM

Clin Pharmacol Ther, 2008; 83(1): 181-3

Clinical trials address questions regarding drug safety for most segments of the population while pregnant women are considered “orphaned” with regards to this issue. Chambers and colleagues believe the lack of adequate pregnancy safety information for the vast majority of medications, combined with a need to make appropriate treatment decisions and to communicate risk information to a potentially vulnerable population, are some of the most challenging and critical women’s health issues.

Clinical implications of increased congenital malformations after first trimester exposures to angiotensin-converting enzyme inhibitors

Cooper WO

J Cardiovasc Nurs, 2008; 23(1): 20-4

Angiotensin-converting enzyme (ACE) inhibitors are contraindicated during the second half of pregnancy because prior studies have shown that their use in late pregnancy can cause oligohydramnios, fetal growth restriction, skull defects, infant anuria and renal failure, and death. Little was known about the effects of ACE inhibitors when taken early during pregnancy. The ACE Inhibitors in Early Pregnancy study aimed to clarify the safety of the use of ACE inhibitors during pregnancy by conducting an epidemiologic study using a large Medicaid database in which medications prescribed for pregnant women as a part of routine care and infant outcomes were studied. In the study, among 209 infants with first trimester exposure to ACE inhibitors, 7.1% had any major congenital malformation. Compared with 29,096 infants with no exposure to any antihypertensive medication, among whom 2.6% had any major congenital malformation, the adjusted risk of major congenital malformations was increased more than 2-fold. The risks of any congenital malformations and risks of specific organ system malformations, including cardiac malformations, were not increased in 202 infants with first trimester exposure to other antihypertensives when compared with infants with no antihypertensive exposure. Cooper concludes that further information on the pregnancy risks of ACE inhibitors and almost every other medication potentially used by pregnant women is needed. Until such information is available, alternative medications to ACE inhibitors should be considered in women of child-bearing age, who are pregnant or who are likely to become pregnant while taking the medication.

Safety and efficacy of blue cohosh (*Caulophyllum thalictroides*) during pregnancy and lactation

Dugoua JJ, Perri D, Koren G, et al

Can J Clin Pharmacol, 2008; 15(1): e66-73

The objective of this study was to systematically review the literature for evidence on the use, safety and pharmacology of blue cohosh, focusing on issues pertaining to pregnancy and lactation. According to a survey of midwives in the United States, approximately 64% of midwives reported using blue cohosh as a labour-inducing aid. There are three case reports in the scientific literature that blue cohosh taken at the time of delivery may cause; 1) perinatal stroke, 2) acute myocardial infarction, profound congestive heart failure and shock and 3) severe multi-organ hypoxic injury. There is one case report that blue cohosh possesses abortifacient properties. There is in vitro evidence that blue cohosh may have teratogenic, embryotoxic and oxytocic effects. In lactation, the safety of blue cohosh is unknown. Based on the available scientific information, the authors conclude that blue cohosh should be used with extreme caution during pregnancy, be used only under medical professional supervision, and not be available to the public as an over-the-counter product. There is an urgent need to conduct a retrospective or prospective cohort study of midwives using blue cohosh in order to determine its safety.

Safety and efficacy of chastetree (*Vitex agnus-castus*) during pregnancy and lactation

Dugoua JJ, Seely D, Koren G, et al

Can J Clin Pharmacol, 2008; 15(1): e74-9

The objective of this study was to systematically review the literature for evidence on the use, safety and pharmacology of chastetree, focusing on issues pertaining to pregnancy and lactation. Results show that in pregnancy, there is poor evidence based on theoretical and expert opinion and in vitro studies that chastetree may have estrogenic and progesteric activity, uterine

stimulant activity, emmenagogue activity and prevent miscarriages. In lactation, theoretical and expert opinion conflict as to whether chastetree increases or decreases lactation. Due to its common use among women of childbearing age, it is likely that some women may consume chastetree while unknowingly pregnant. Dugoua and colleagues conclude that complementary and alternative medicine, midwifery and medical practitioners should be aware of this fact when prescribing chastetree to women of childbearing age, particularly when the patient is planning a family.

Safety and efficacy of cranberry (vaccinium macrocarpon) during pregnancy and lactation
Dugoua JJ, Seely D, Koren G, et al
Can J Clin Pharmacol, 2008; 15(1): e80-6

The objective of this study was to systematically review the literature for evidence on the use, safety and pharmacology of cranberry, focusing on issues pertaining to pregnancy and lactation. Results show that there is no direct evidence of safety or harm to the mother or fetus as a result of consuming cranberry during pregnancy. In lactation, the safety or harm of cranberry is unknown. Given the evidence to support the use of cranberry for urinary tract infections and its safety profile, Dugoua and colleagues conclude that cranberry supplementation as fruit or fruit juice may be a valuable therapeutic choice in the treatment of urinary tract infections during pregnancy.

Cognitive assessment of children at age 2(1/2) years after maternal fish oil supplementation in pregnancy: a randomized controlled trial
Dunstan JA, Simmer K, Dixon G, et al
Arch Dis Child Fetal Neonatal Ed, 2008; 93(1): F45-50

The aim of this study was to assess the effects of antenatal omega 3 long-chain polyunsaturated fatty acid (n-3 LC PUFA) on cognitive development in a cohort of children whose mothers received high-dose fish oil in pregnancy. Dunstan and colleagues conclude that maternal fish oil supplementation during pregnancy is safe for the fetus and infant, and may have potentially beneficial effects on the child's eye and hand coordination. Further studies are needed to determine the significance of this finding.

Impact of the use of antenatal corticosteroids on mortality, cerebral lesions and 5-year neurodevelopmental outcomes of very preterm infants: the EPIPAGE cohort study
Foix-L'Hélias L, Marret S, Ancel PY, et al
BJOG, 2008; 115(2): 275-82

The purpose of this study was to assess the impact of antenatal corticosteroids (ACS) on neonatal mortality, cerebral lesions and 5-year neurodevelopmental outcome of infants born at 24-27 and 28-32 weeks of gestational age. The results show that ACS therapy greatly increases the survival of very preterm infants, including the most immature. However, there is little evidence that ACS therapy affects long-term neurodevelopmental and behavioural outcome in 28- to 32-week survivors, and none in <28-week survivors.

Effect of preterm birth and antenatal corticosteroid treatment on lactogenesis II in women
Henderson JJ, Hartmann PE, Newnham JP, et al
Pediatrics, 2008; 121(1): e92-100

The onset of copious milk secretion after birth is known as lactogenesis II. The objective of this study was to investigate the effect of preterm birth and antenatal corticosteroids on the timing of

lactogenesis II after birth. Women who had received antenatal betamethasone treatment and were expressing for a preterm infant whose gestational age was <34 weeks (N = 50) were studied. On days 1 to 10 postpartum, participants measured the volume of milk expressed in 24-hour periods and collected milk samples. Lactose and citrate levels were analyzed in the milk. According to the researchers, delivery at extremely preterm gestational ages caused a significant delay in the onset of lactogenesis II. The volume of milk was reduced further when antenatal corticosteroids were administered between 28 and 34 weeks' gestation and delivery occurred 3 to 9 days later. Henderson and colleagues conclude that in view of the advantages of mothers' own milk, additional support with lactation is recommended for mothers of preterm infants, particularly those who have been treated with corticosteroids before the delivery.

Hyperemesis in pregnancy: an evaluation of treatment strategies with maternal and neonatal outcomes

***Holmgren C, Aagaard-Tillery KM, Silver RM, et al
Am J Obstet Gynecol, 2008; 198(1): 56.e1-4***

The purpose of this study was to evaluate the use of interventions such as a peripherally inserted central catheters (PICC) line or nasogastric (NG)/nasoduodenal (ND) tube with the use of medications alone in the management of pregnancies with hyperemesis. Holmgren and colleagues conclude that maternal complications associated with PICC line placement are substantial despite no difference in neonatal outcomes, suggesting that the use of PICC lines for treatment of HEG patients should not be routinely used.

Informing patients of the teratogenic potential of mood stabilizing drugs: a case note review of the practice of psychiatrists

***James L, Barnes TR, Lelliott P, et al
J Psychopharmacol, 2007; 21(8): 815-9***

Lithium, carbamazepine and valproate are established human teratogens. Women of childbearing potential who are prescribed these drugs should be informed of their teratogenic potential and advised of the need for adequate contraception and the protective role of folate. The authors reviewed the clinical records of all women of childbearing age in long-term contact with one specialist mental health Trust providing services for a total population of 750,000. One hundred and thirty-eight (16%) of 837 women of childbearing age were prescribed one or more of these drugs. There was documented evidence that 21% of these women had been informed about teratogenicity and that 24% had been advised about contraception. Fourteen women (10%) had a confirmed pregnancy while taking lithium, carbamazepine or valproate; eight had a complication of pregnancy. If prescribing practice in this large mental health Trust were typical of the UK, between 7,000 and 11,000 women of childbearing potential would be prescribed lithium, carbamazepine or valproate by psychiatrists without documented discussion of the risks.

Methadone maintenance and breastfeeding in the neonatal period

***Jansson LM, Choo R, Velez ML, et al
Pediatrics, 2008; 121(1): 106-14***

In a sample of methadone-maintained breastfeeding women and a matched group of formula-feeding women, this study evaluated concentrations of methadone in breast milk among breastfeeding women and concentrations of methadone in maternal and infant plasma in both groups. Results show that concentrations of methadone in breast milk were low (range: 21.0-462.0 ng/mL) and not related to maternal dose. There was a significant increase in methadone concentrations in breast milk over time for all 4 sampling times. Concentrations of methadone in

maternal plasma were not different between groups and were unrelated to maternal dose. Concentrations of methadone in infant plasma were low (range: 2.2-8.1 ng/mL) in all samples. The infants in both groups underwent neurobehavioral assessments on days 3, 14, and 30; and no significant effects of breastfeeding on neurobehavioral outcomes were found. Fewer infants in the breastfed group required pharmacotherapy for neonatal abstinence syndrome, but this was not a statistically significant finding. Jansson and colleagues conclude that the results of their study contribute to the recommendation of breastfeeding for methadone-maintained women.

Antiepileptic drug use, folic acid supplementation, and congenital abnormalities: a population-based case-control study

***Kjaer D, Horvath-Puhó E, Christensen J, et al
BJOG, 2008; 115(1): 98-103***

The objective of this study was to investigate whether folic acid supplementation in early pregnancy modifies the association between the prevalence of congenital abnormalities in the offspring and maternal use of carbamazepine, phenobarbital, phenytoin, and primidone. The results indicate that the risk of congenital abnormalities in children exposed in utero to carbamazepine, phenobarbital, phenytoin, and primidone is reduced but not eliminated by folic acid supplementation at 5-12 weeks from the first day of the last menstrual period. The researchers conclude that the statistical precision in their study is limited due to rarity of the exposures, and further studies are needed.

Impact of patent ductus arteriosus and subsequent therapy with indomethacin on cerebral oxygenation in preterm infants

***Lemmers PM, Toet MC, van Bel F
Pediatrics, 2008; 121(1): 142-7***

The purpose of this study was to investigate the impact of patent ductus arteriosus and its treatment with indomethacin on regional cerebral oxygen saturation and fractional tissue oxygen extraction by using near-infrared spectroscopy. Lemmers and colleagues conclude that a hemodynamically significant patent ductus arteriosus has a negative effect on cerebral oxygenation in the premature infant. Subsequent and adequate treatment of a patent ductus arteriosus may prevent diminished cerebral perfusion and subsequent decreased oxygen delivery, which reduces the change of damage to the vulnerable immature brain.

Use of medications for gastroesophageal reflux at discharge among extremely low birth weight infants

***Malcolm WF, Gantz M, Martin RJ, et al
Pediatrics, 2008; 121(1): 22-7***

The three main goals for this study are as follows: (1) to determine the use of medications to treat gastroesophageal reflux in extremely low birth weight infants (birth weight of < 1000 g) at discharge; (2) to identify risk factors associated with the use of medications to treat gastroesophageal reflux at discharge; and (3) to assess the contribution of gastroesophageal reflux medication use at discharge to growth and development at corrected ages of 18 to 22 months. Results reveal that the use of antireflux medications at the time of discharge seem to be common for extremely low birth weight infants (especially those discharged at postmenstrual age of > 42 weeks) but does not seem to have effects on growth or development at the time of follow-up evaluations.

Benefit of magnesium sulfate given before very preterm birth to protect infant brain
Marret S, Marpeau L, Bénichou J
Pediatrics, 2008; 121(1): 225-6

No abstract available.

Neonatal outcome following pregnancy exposure to antidepressants: a prospective controlled cohort study
Maschi S, Clavenna A, Campi R, et al
BJOG, 2008; 115(2): 283-9

The purpose of this study was to determine the incidence of early adverse effects associated with antidepressant drug use during pregnancy. The authors selected women who took antidepressants during pregnancy and delivered liveborn children between 1995 and 2003. Each case was matched for maternal age and gravidity to six randomly selected controls (not exposed to teratogenic drugs or drugs known to cause neonatal side effects). Odds ratio was estimated for attributable risks. Of the 200 neonates exposed to antidepressants in utero, 14 had adverse events and 3 required Special Care Unit admission. Jaundice (n = 5), agitation (n = 3) and respiratory distress (n = 2) were the most common symptoms. In the control group, 50 newborns had side effects and no statistically significant differences in the prevalence rate compared to the exposed group were found, even after stratification for drugs and pregnancy period of exposure. Only the prematurity rate was significantly higher in exposed compared to non-exposed newborns (OR = 2.31; 95% CI 1.14-4.63). Maschi and colleagues conclude these results do not support an association between antidepressant exposure and unsafe fetal and neonatal outcomes in newborns. However, a collaborative international multicentre epidemiological monitoring of the use of psychotropic drugs during pregnancy is needed in order to guarantee pregnant women and their children safe and effective treatments, both at brief and long time from exposure.

Preinduction cervical ripening with prostaglandin E2 at preterm
Melamed N, Yogev Y, Hadar E, et al
Acta Obstet Gynecol Scand, 2008; 87(1): 63-7

The objective of this study was to evaluate the efficacy of prostaglandin E2 (PGE2) for cervical ripening at preterm and to identify factors predicting ripening failure. The researchers conclude that the use of PGE2 for preinduction cervical ripening at preterm may be associated with an increased risk of ripening failure and caesarean section compared with term gestations. This information may be useful when consulting women regarding the available options when premature delivery is necessary.

Amoxicillin pharmacokinetics in pregnant women with preterm premature rupture of the membranes
Muller AE, DeJongh J, Oostvogel PM, et al
Am J Obstet Gynecol, 2008; 198(1): 108.e1-6

The aim of this study was to examine the pharmacokinetics of intravenously administered amoxicillin in pregnant women with preterm premature rupture of the membranes. Muller and colleagues conclude that the pharmacokinetics of amoxicillin in pregnant patients with preterm premature rupture of the membranes is similar to nonpregnant individuals. Given the small interindividual variability in pharmacokinetics, no dose adjustments are required to account for difference between subjects under normal circumstances.

Maternal and fetal effects of systemic therapy in the pregnant woman with cancer

Pereg D, Lishner M

Recent Results Cancer Res, 2008; 178: 21-38

No abstract available.

In utero exposure to mycophenolate mofetil: a characteristic phenotype?

Perez-Aytes A, Ledo A, Boso V, et al

Am J Med Genet A, 2008; 146(1): 1-7

Perez-Aytes and colleagues present a case of a newborn patient, born to a recipient of renal transplantation, who became pregnant while taking mycophenolate mofetil (MMF) as immunosuppressive therapy. The newborn exhibited cleft lip and palate, bilateral microtia and atretic external auditory canals, chorioretinal coloboma, hypertelorism, and micrognathia. An extensive review of the literature documented six other cases with similar malformations after in utero exposure to MMF. A consistent pattern of malformations comprising cleft lip and palate, microtia and external auditory canals could be observed in five of the six cases. A different malformative pattern observed in one of the patients could be attributed to a different agent rather than MMF. The possible teratogenic effects of other immunosuppressive drugs, such as tacrolimus and prednisone, to which this patient was also exposed, are discussed herein. In addition, the differential diagnosis with other dysmorphic syndromes that can present with a similar phenotype, such as CHARGE syndrome, 18q deletion and hypertelorism-microtia-clefting (HMC) syndrome, is presented. The authors conclude that in utero exposure to MMF can cause a characteristic phenotype and propose the existence of a mycophenolate-associated embryopathy whose main features are: cleft lip and palate, microtia with atresia of external auditory canal, micrognathia and hypertelorism. Ocular anomalies, corpus callosum agenesis, heart defects, kidney malformations, and diaphragmatic hernia may be part of the phenotypic spectrum of MMF embryopathy. The human teratogenicity of MMF is reinforced by this report, and the current contraceptive recommendations about its use in fertile women are stressed.

Postnatal hydrocortisone treatment for chronic lung disease in the preterm newborn and long-term neurodevelopmental follow-up

Rademaker, KJ, deVries LS, Uiterwaal CS, et al

Arch Dis Child Fetal Neonatal Ed, 2008; 93(1): F58-63

This review examines the literature on postnatal hydrocortisone treatment for chronic lung disease in preterm-born infants with a particular focus on the effects of such treatment on long-term neurodevelopmental outcomes. Quantitative published evidence does not point to a clear advantage of treatment with hydrocortisone over dexamethasone with regard to the impact on long-term neurological outcomes. According to Rademaker and colleagues, in the absence of a randomized comparison, a consensus may soon have to be reached on the basis of the best available evidence whether hydrocortisone should replace dexamethasone in the treatment of chronic lung disease.

The extension of epidural blockade for emergency Caesarean section: a survey of current UK practice

Regan KJ, O'Sullivan G

Anaesthesia, 2008; 63(2): 136-42

The conversion of epidural analgesia during labour to surgical anaesthesia for Caesarean section can have important medical and medicolegal implications. This survey of lead obstetric anaesthetists in the U.K. sought to establish the current management for extending epidural blockade for emergency Caesarean section. Of those surveyed 68% give the full dose of the local anaesthetic mixture in the delivery room, whilst 12.5% initiate the top-up in the delivery room and give the remainder of the dose in theatre. Fifteen per cent transfer the woman to theatre before commencing anaesthesia and 34% give a test dose before the full anaesthetic dose. Guidelines for converting labour analgesia to anaesthesia for emergency Caesarean section were available in 64% units. Bupivacaine 0.5% was the most commonly used agent, being used as the sole agent by 41.5% units and in combination by a further 18%. Adrenaline was added to the chosen local anaesthetic by 30%, whilst 12% added bicarbonate. In all, 13 combinations of local anaesthetics and adjuncts were used. The mode time to transfer the patient to theatre was 1 min. Of the 161 respondents who commenced anaesthesia in the delivery room, 71% did not monitor the patient during transfer, whilst 87% had ephedrine immediately available. Thirty-three respondents reported a total of 43 adverse incidents associated with the extension of epidural blockade. These included high blocks, inadequate blocks and possible intravascular injections, the latter resulting in two seizures and one cardiac arrest.

Early thimerosal exposure and neuropsychological outcomes

Rooney JP

N Engl J Med, 2008; 358(1): 93-4; author reply 94

No abstract available.

Folic acid and prevention of neural tube defects

Ryan-Harshman M, Aldoori W

Can Fam Physician, 2008; 54(1): 36-8

This article answers the following question: Now that flour and pasta have been fortified with folic acid in Canada, do I still need to recommend folic acid supplements to my patients who are of child-bearing age? If I should recommend supplements, when should I recommend them, and what is an appropriate dose? According to the authors, non-pregnant women should consume 400 microg of folic acid daily, and pregnant women should consume 600 microg of folic acid daily. Mean intakes of folate in Canada before fortification were approximately 200 microg/d or less. Fortification increased intake of folic acid by up to 100 microg/d. Doctors should discuss the importance of folic acid with patients who are planning pregnancy and it is recommended that a folic acid supplement or prenatal multivitamin containing at least 400 microg of folic acid be consumed daily. Women in intermediate- to high-risk categories for neural tube defects, such as a previous neural tube defect-affected pregnancy, should take 4 to 5 mg of folic acid daily.

Safety and efficacy of Panax ginseng during pregnancy and lactation

Can J Clin Pharmacol, 2008; 15(1): e87-94

Seely D, Dugoua JJ, Koren G, et al

The objective of this study was to systematically review the literature for evidence on the use, safety and pharmacology of Panax ginseng, focusing on issues pertaining to pregnancy and lactation. Seely and colleagues conclude that Panax ginseng should be consumed with caution during pregnancy, especially during the first trimester, and during lactation.

Trastuzumab treatment for breast cancer during pregnancy
Shrim A, Garcia-Bournissen F, Maxwell C, et al
Can Fam Physician, 2008; 54(1): 31-2

This article discusses the consequences of trastuzumab treatment during pregnancy. According to the researchers, human data regarding the safety of trastuzumab during pregnancy are scarce. Anhydramnios was observed in a case where the exposure to trastuzumab occurred during the second trimester, which reversed after discontinuation of the drug without any apparent consequences to the baby. Evidence is insufficient to provide any recommendations, but in light of the case reports, pregnancies exposed to trastuzumab during the second trimester should be closely followed with particular attention to amniotic fluid volume.

[Ginger, pregnancy nausea and possible fetal injuries (testosterone effect)]
Søndergaard K.
Ugeskr Laeger, 2008; 170(5): 359; author reply 359

No abstract available.

Effect of maternal multiple micronutrient supplementation on fetal loss and infant death in Indonesia: a double-blind cluster-randomised trial
Supplementation with Multiple Micronutrients Intervention Trial (SUMMIT) Study Group,
Shankar AH, Jahari AB, et al
Lancet, 2008; 371(9608): 215-27

Maternal nutrient supplementation in developing countries is generally restricted to provision of iron and folic acid (IFA). Change in practice toward supplementation with multiple micronutrients (MMN) has been hindered by little evidence of the effects of MMN on fetal loss and infant death. The authors of this study assessed the effect of maternal supplementation with MMN, compared with IFA, on fetal loss and infant death in the setting of routine prenatal care services. Results show that maternal MMN supplementation, as compared with IFA, can reduce early infant mortality, especially in undernourished and anaemic women. Shankar and colleagues conclude that maternal MMN supplementation may therefore be an important part of overall strengthening of prenatal-care programmes.

Down the primrose path: petechiae in a neonate exposed to herbal remedy for parturition
Wedig KE, Whitsett JA
J Pediatr 2008, 152(1): 140, 140.e1

No abstract available.

Folic acid supplementation in early second trimester and the risk of preeclampsia
Wen SW, Chen XK, Rodger M, et al
Am J Obstet Gynecol, 2008; 198(1): 45.e1-7

The objective of this study was to evaluate the association between folic acid supplementation in early second trimester and preeclampsia risk. Results reveal that supplementation of vitamins containing folic acid was associated with increased serum folate, decreased plasma homocysteine, and reduced risk of preeclampsia.

Clinical inquiries. What is the most effective and safe malaria prophylaxis during pregnancy?
Wiltz SA, Crawford P, Nichols W
J Fam Pract, 2008; 57(1): 51-3

No abstract available.

LAY PRESS NEWS

Immunosuppressant drug associated with prenatal defects
Asian News International, 2008; February 7

A new study led by Dr. Antonio Perez-Aytes and Dr. Maximo Vento has cited that infants born to a kidney transplant recipient mother who had taken an immunosuppressant drug, called mycophenolate mofetil may have specific birth defect patterns specific to this drug. The findings of the study suggest that mycophenolate mofetil, commercially available as CellCept, have potentially harmful effects on the foetus and may result in defects like cleft lip and palate, as well as defects of the jaw, eyes and ears and no external ear canals. A similar pattern of birth defects was seen in previous reports of birth defects in infants who were exposed to mycophenolate mofetil in utero. The study described these infants, noting that the pattern of cleft lip/palate and ear malformations was seen in every case but one. While such defects of the eye had not been seen in humans before, studies in rats and rabbits have shown ocular malformations following exposure to mycophenolate mofetil. According to Dr. Vento, "The patient needs to be adequately counseled, and withdrawn from immunosuppressants that may be deleterious to the baby within sufficient of becoming pregnant to avoid any interference during the first 12 weeks of gestation."

Pregnant women rarely use smoking cessation meds
Reuters Health E-Line, 2008; February 6

Women rarely opt to take smoking cessation medication during pregnancy, researchers report. But pregnant women may be more likely to use smoking cessation medications if their obstetric providers routinely discussed use of these medications and health insurance covered the cost, suggests Dr. Nancy A. Rigotti, of Massachusetts General Hospital, Boston, and colleagues. The investigators analyzed data collected from 296 pregnant smokers participating in a smoking cessation trial from 2001 to 2004. The women were an average of 29 years of age and smoked about 10 cigarettes a day when they enrolled in the study. In end-of-pregnancy telephone surveys, the women reported that 26.5 percent of their obstetric providers discussed nicotine replacement and 12.2 percent discussed the use of bupropion for smoking cessation during pregnancy, Rigotti and colleagues report in *Obstetrics and Gynecology*. Overall, 7.4 percent of the women used nicotine replacement during pregnancy and another 3.4 percent used the smoking cessation drug bupropion. Three months after delivery, 23.4 percent of the women reported discussing nicotine replacement while 16.5 percent said their obstetric provider discussed bupropion. At this point, the use of nicotine replacement increased to 8.8 percent while 7.1 percent of the women reported using bupropion. For each medication the investigators saw a statistically significant association between a provider's discussion of that medication and a pregnant smoker's use of the medication. Having insurance cover the cost of cessation medication, older age, living with a partner, a previous birth, and higher levels of education were also associated with cessation medication use. U.S. and British clinical practice guidelines recommend nicotine replacement for pregnant smokers provided the nicotine dose from replacement therapy does not exceed the level obtained from smoking. Bupropion is similarly recommended by U.S. but not British guidelines, the researchers note. Still, obstetricians and pregnant women appear more reluctant to consider

cessation medications than clinical guidelines recommend, the investigators report. They suggest that clearer efficacy and safety data from clinical trials may ease this reluctance.

HIV drugs make breast-feeding safer
Reuters, 2008; February 4

Babies of HIV-infected women who were given the drug nevirapine while they breast-fed were half as likely to become infected, researchers told a meeting in Boston of AIDS experts. A single dose of nevirapine given to the mother as she goes into labor and to the baby at birth can reduce transmission by 47 percent. However, as the virus can be carried through their mother's milk, babies continue to become infected after birth. Dr. Brooks Jackson of John Hopkins University and colleagues tested whether they could safely continue giving the drug to babies for as long as six weeks. Nevirapine or a vitamin solution was administered to 2,000 new babies between 2001 and 2007. Results showed that at 6 months of age, the risk of postnatal HIV infection or death in infants who received the six-week regimen was almost one-third less than the risk for infants given only a single dose.

Study finds a simple way to avoid cerebral palsy: Epsom salts
Fisher JP
The News & Observer, 2008; February 1

A study conducted at the University of North Carolina Hospitals, Wake Forest Baptist University Medical Center and 18 other medical centers around the country found that giving women in early labor magnesium sulfate infusions reduced by nearly half the number of premature babies born with serious cases of cerebral palsy. Dr. John Thorp and colleagues treated 947 women in early labor with infusions of the study drug and gave 655 women in a control group drips of an inactive solution; the remainder of women in the study were ineligible for treatment, often because they delivered their babies too quickly for intervention. All the women were between 28 and 31 weeks into their pregnancies. Magnesium sulfate did not affect rates of death among babies born to women in either group. Researchers observed a significant difference in cerebral palsy rates. Treatment with magnesium sulfate did not have serious side effects in women or their babies. Dr Thorp said UNC Hospitals is already offering magnesium sulfate to women in premature labor. He hopes more hospitals will do the same.

Pregnant mothers prescribed high-risk drug
Chitrodia RB
The Times of India, 2008; February 1

There are fears that some manufacturers of oral progesterone – the hormone administered to support high-risk pregnancy – are promoting the drug as a “tonic” even for normal pregnancy. A recent Monthly Index of Medical Specialties (MIMS) editorial by Dr. Chandra Gulati, states, “In its package insert, a Mumbai-based company is advising doctors to use its brand ‘to help pregnancy’, whatever it means.” In other words, it is being prescribed for patients with no documented deficiency of progesterone. If used in early pregnancy, the MIMS editorial says, progesterone can cause congenital anomalies including hare lip and heart defects. A latest US study suggested at least a two-fold rise in risk of hypospadias (a uro-genital defect) among boys born by mothers who took progesterone before or during early pregnancy.

Unborn in drugs danger
Daily Telegraph, 2008; January 23

Pregnant women are being forced to take potentially dangerous drugs because pharmaceutical companies are not developing medications that are proven to be safe for unborn babies, a new report warns. A major review of international drug development penned by a leading Australian researcher has labeled pregnancy a "pharma-free" wasteland, with virtually no new drugs on the horizon. Professor Nicholas Fisk, from the University of Queensland, blames the drug dearth on the expense of reproductive trials and major disasters such as Thalidomide, a German drug responsible for severe deformities in 10,000 babies born in the 1950s and 1960s. As a result women needing drugs for pregnancy, labour, abortion or other obstetric conditions must almost routinely resort to so-called off-licence medications that have not been officially tested, Professor Fisk said. A search of drug databases found that only 17 of the 37,000 drugs under development worldwide since 1981 were for maternal health indications. Yet worldwide there are over half a million maternal and seven million perinatal deaths a year. "It is high time to address this failure," Professor Fisk said.

Daily Double can be fatal to fetus: study
Kirkey S
National Post, 2008; January 21

According to a new study, just 2 cups of coffee a day doubles a pregnant women's risk of miscarriage. Dr. Li's and colleagues recruited 1,063 San Francisco women from October 1996 to October 1998. Women were recruited early in their pregnancy - as early as four weeks gestation - so the research was able to capture a lot of miscarriages that most studies overlook. As caffeine readily crosses the placental barrier, the pregnant women were asked about their caffeine consumption and their changing pattern of drinking. They were also asked about nausea and vomiting and other factors that might influence the amount of caffeine they consumed. Overall, 172 women, or 16% miscarried. The higher the intake of caffeine from any source - coffee, tea, caffeine-containing soft drinks or hot chocolate - the greater the risk of early or late miscarriage. Compared with non-users, women who consumed 1-200mg caffeine daily had an increased risk of miscarriage (15% versus 12%). The risk was higher (25%) in women who consumed more than 200mg of caffeine daily.

Avoid two foreign products
Montreal Gazette, 2008; January 11

Health Canada is warning consumers about the potentially dangerous side effects of a product for stimulating lactation in pregnant and nursing women. They are advising women not to use a product called Galactogil bearing specific lot numbers and expiry dates because of bacterial contamination that could cause pneumonia and blood poisoning. Manufactured in France by the IPRAD Group, Galactogil is promoted as a natural product for pregnant or nursing mothers and is not authorized for sale here. Health Canada says they may have been purchased by people travelling abroad or over the Internet.