

# CaseMed-Pregnancy Resource Newsletter

## May 2008

### MEDICAL STUDIES

#### ***Breast Cancer; Pregnant patients lose out in breast cancer treatment; a new approach is needed***

*No authors listed*

***OBGYN & Reproduction Week, 2008; April 28***

Pregnant breast cancer patients can be treated as closely as possible to existing guidelines for non-pregnant patients, with few ill effects, a scientist told the 6th European Breast Cancer Conference (EBCC-6). Dr. Sibylle Loibl, Assistant Professor in Obstetrics and Gynaecology at University of Frankfurt, Germany, and a member of the German Breast Group, said that until now, evidence upon which decisions on treatment for pregnant patients could be made was limited, and that a cautious approach by doctors meant that many women did not get the best treatment for their cancer. "We realized that there are hardly any data on this subject," she said, "and therefore set out to collect information from patients in Germany and throughout Europe." The German Breast Group launched a data-collection exercise in 2003. Information on 122 pregnant patients diagnosed with breast cancer between April 2003 and December 2007 was analyzed for a number of factors – foetal outcome four weeks after delivery, maternal outcome of pregnancy, stage and biological characteristics of the breast cancer, breast cancer therapy, sensitivity and specificity of diagnostic procedures, outcome of the child five years later, and outcome of the breast cancer five years after diagnosis. The median gestational age at the time of diagnosis was 21 weeks, and the median age of the women 33 years. Some patients chose not to continue the pregnancy on learning of their diagnosis, but of those who did, 33.3% received surgery only, 43.2% were treated by surgery and chemotherapy, 5.4% by chemotherapy alone, and 2.7% had no treatment at all. The median time for delivery was 36 weeks, slightly earlier than that which is normal in healthy women. Although there were some health problems among the newborn babies, they were generally minor, and the foetal outcome in babies whose mothers received chemotherapy was not different to those whose mothers did not. "We are still analyzing some of the data," said Dr. Loibl, "but in terms of our primary endpoint, foetal outcome four weeks after delivery, we are able to say that this shows that pregnant patients can benefit from the same breast cancer treatment that is given to non-pregnant women, and that this should be done in standardized multidisciplinary teams. Later this year we hope to have collected 200 patients in the dataset. This will be the largest ever data collection concerning breast cancer during pregnancy, and we intend to follow up these women and their children over a long period of time to produce further information."

#### ***Epilepsy; Breastfeeding while taking seizure medicine does not appear to harm children***

*No authors listed*

***OBGYN & Reproduction Week, 2008; April 28***

Research to be presented at the American Academy of Neurology 60th Anniversary Annual Meeting in Chicago, April 12–19, 2008 reveals that breastfeeding while taking seizure

medications does not appear to harm a child's cognitive development. Researchers tested the cognitive development of 187 two-year-old children whose mothers were taking the epilepsy drugs lamotrigine, carbamazepine, phenytoin, or valproate. Forty-one percent of the children were breastfed. The study found breastfed children had higher cognitive test scores than those children who were not breastfed, and this trend was consistent for each anti-epilepsy drug. The children who were breastfed received an average test score of 98.1 compared to a score of 89.5 for the children not breastfed. However, the results were not significant after adjusting for the mother's IQ. Thus, it appears that the higher scores in children who were breastfed are due to the fact that their mothers had higher IQs. Study author Kimford Meador says animal studies have shown that some anti-epilepsy drugs, but not all, can cause cells to die in immature brains, but this effect can be blocked by the protective effects of beta estradiol, which is the mother's sex hormone. "Since the potential protective effects of beta estradiol in utero are absent after birth, concern was raised that breastfeeding by women taking anti-epilepsy drugs may increase the risk of anti-epilepsy drug-induced cell death and result in reduced cognitive outcomes in children." Meador says additional research on the effects of breastfeeding should be extended to other anti-epilepsy drugs and mothers who use more than one anti-epilepsy medication. The study is part of an ongoing study of the long-term effects of in utero anti-epilepsy drug exposure on children's cognition. Women with epilepsy who were taking anti-epilepsy drugs were enrolled in the study during pregnancy. Ultimately, the study will examine the effects of in utero anti-epilepsy drug exposure on children at six years old.

***Revised guidelines for antiretroviral use in pregnant women***

***No authors listed***

***AIDS Clin Care, 2008; 20(2): 11***

No abstract available.

***ACOG Committee Opinion No. 402: Antenatal corticosteroid therapy for fetal maturation***

***American College of Obstetricians and Gynecologists Committee on Obstetric Practice***

***Obstet Gynecol, 2008; 111(3): 805-7***

No abstract available.

***Prescribing in pregnancy and lactation***

***Begg EJ***

***Br J Clin Pharmacol, 2008; 65(5): 627-8***

No abstract available.

***Prospective randomised comparative study of the effect of buprenorphine, methadone and heroin on the course of pregnancy, birthweight of newborns, early postpartum adaptation and course of the neonatal abstinence syndrome (NAS) in women followed up in the outpatient department***

***Binder T, Vavrinková B***

***Neuro Endocrinol Lett, 2008; 29(1): 80-6***

The aim of this study was to evaluate the effect of substitution therapy in heroin addicted pregnant women on the course of pregnancy, perinatal outcomes and course of the neonatal abstinence syndrome. Results showed that the comparison of groups of outpatients is in many ways questionable because of the restricted possibility of the patients' control. The lifestyle of addicted women has the same impact as the drug use alone. This is probably the main reason for

differences in some of the monitored parameters between individual groups. Based on the results of this study, the researcher's believe that substitution therapy provides pregnant women with the possibility of social stabilization and adequate prenatal care. Substitution therapy decreases the street heroin consumption. Methadone notably protracts the newborn's abstinence syndrome. With regard to this fact, attention has been recently focused on substitution with buprenorphine that seems to be from this viewpoint a more considerate option.

***Asthma exacerbations during the first trimester of pregnancy and the risk of congenital malformations among asthmatic women***

***Blais L, Forget A***

***J Allergy Clin Immunol, 2008; Apr 12 [Epub ahead of print]***

The purpose of this study was to investigate whether asthmatic women who had an exacerbation during the first trimester of pregnancy were more at risk of having a baby with a congenital malformation. Blais and Forget conclude that asthma exacerbations during the first trimester of pregnancy were found to significantly increase the risk of a congenital malformation.

***High-dose carisoprodol during pregnancy and lactation***

***Briggs GG, Ambrose PJ, Nageotte MP, et al***

***Ann Pharmacother, 2008; May 6 [Epub ahead of print]***

The objective of this study was to report a case of high-dose carisoprodol during pregnancy and breastfeeding. The subject of this study was a 28-year-old woman with severe back muscle spasm who took carisoprodol 2800 mg/day before and throughout an uncomplicated pregnancy and while exclusively breast-feeding her infant during the first month after birth. Briggs and colleagues conclude that except for mild sedation, no other toxicity was observed in a near-term infant exposed to carisoprodol throughout gestation and during breastfeeding in the first month after birth.

***Respiratory compromise after MgSO<sub>4</sub> therapy for preterm labor in a woman with myotonic dystrophy: a case report***

***Catanzarite V, Gambling D, Bird LM, et al***

***J Reprod Med, 2008; 53(3): 220-2***

This study describes the case of a 35-year-old woman who was hospitalized with suspected mild myotonic dystrophy, polyhydramnios and preterm labor at 33 weeks. MgSO<sub>4</sub> infusion rapidly resulted in respiratory compromise. After the infusion was stopped, muscular strength returned to baseline. Both the mother and infant proved to have myotonic dystrophy. Catanzarite and colleagues conclude that the choice of tocolytic medication in maternal myotonic dystrophy is problematic. Beta-2 sympathomimetics have been reported to precipitate myotonia. This particular case illustrates the potential for MgSO<sub>4</sub> to cause respiratory embarrassment. Indomethacin may be the tocolytic of choice in myotonic dystrophy.

***Persistent pulmonary hypertension of the newborn following ingestion of nonsteroidal anti-inflammatory drugs during pregnancy***

***[Article in Spanish]***

***Chacón AR, Menéndez HC, Chimenti CP, et al***

***An Pediatr (Barc); 2008; 68(4): 357-60***

Nonsteroidal anti-inflammatory drugs induce the inhibition of prostaglandin synthesis, which can cause constriction of the fetal ductus arteriosus in pregnancy. In this study, Chacón and

colleagues report two cases of antenatal closure of ductus arteriosus with severe pulmonary hypertension following maternal ingestion of nonsteroidal anti-inflammatory drugs (niflumic acid and acetylsalicylic acid) in the last days before delivery. According to the researchers, prescribing nonsteroidal anti-inflammatory drugs must be avoided during pregnancy. Fetal echocardiography must be monitored in those women treated with nonsteroidal anti-inflammatory drugs.

***Treatment and prevention of malaria in pregnancy and newborn***

***Coll O, Menendez C, Botet F, et al***

***J Perinat Med, 2008; 36(1): 15-29***

In this article, Coll and colleagues review the pathology, diagnosis, and current recommendations for treatment and prevention of malaria in the pregnant woman and her infant.

***Risk of congenital malformations among infants exposed to antidepressants during pregnancy***

***Davis RL, Andrade S, Platt R***

***Pharmacoepidemiol Drug Saf, 2008; 17(4): 423***

No abstract available.

***Pregnancy in recipients of kidney transplantation: effects on the mother and the child***

***Diaz JM, Canal C, Giménez I, et al***

***Nefrologia, 2008; 28(2): 174-7***

The purpose of this study was to analyze pregnancy after kidney transplantation and the consequences on mother, graft and child. The researchers reviewed ten pregnant women with kidney transplantation, who were on average 29 years old and 44 months post-kidney transplantation. The mean glomerular filtration rate was 64 ml/min and the immunosuppression was with prednisone and tacrolimus. The outcomes of different variables were analyzed before and during pregnancy, and after labour. Diaz and colleagues conclude that pregnancy after kidney transplantation is safe with prednisone and tacrolimus when the renal function is good, proteinuria doesn't exist and blood pressure is controlled.

***Medication errors in obstetrics***

***Kfuri TA, Morlock L, Hicks RW, et al***

***Clin Perinatol, 2008; 35(1): 101-17***

The findings highlighted in this article suggest that obstetricians and perinatologists face several challenges for safe medication use during pregnancy. Furthermore, evidence of in-hospital medication errors from obstetric services has been provided by national medication error data voluntarily submitted from many hospitals. The data provide fresh insight into the nature of medication errors in obstetrics, especially regarding the medication use process, the most common types of errors reported, the most commonly reported products overall, as well as those that resulted in patient harm. Providers and staff working within health care organizations should be well aware that a substantial number of patients experience medication errors which can result in serious injuries.

***Neurological diseases in pregnancy: implications for anesthesia care - part 2***

***[Article in German]***

***Griebe A, Aniset L, Jámbor C, et al***

***Anesthesiol Intensivmed Notfallmed Schmerzther, 2008; 43(3): 190-5***

In the parturient as well as in the pregnant patient with neurological disease, surgery is necessary more frequently than in healthy pregnant women. Most pregnancies of these patients will result in a slightly increased rate for cesarean section. The focus of anesthesia care is mostly to avoid damage to the fetus, in some pathologies to protect the mother. The authors conclude that anesthesia care for the pregnant and the parturient presenting with a neurological disease requires: 1.) expertise with neuroanesthesia and obstetric anesthesia care, 2.) accurate physical examination of the neurological system preoperatively, 3.) safe choice and conductance of the anesthesia technique (mostly regional anesthesia) 4.) avoidance of unfavorable drug effects for the fetus and the nervous system of the mother and 5.) intraoperative neuromonitoring together with the control of the fetal heart rate.

***Providing information regarding exposures in pregnancy: A survey of North American Teratology Information Services***

***Hancock RL, Ungar WJ, Einarson A, et al  
Reprod Toxicol, 2008; Mar 2 [Epub ahead of print]***

Teratology Information Services (TIS) provide information on exposures during pregnancy and breast-feeding. The purpose of this study was to gather descriptive information on current TIS operations. The results were based on detailed surveys completed by sixteen American and two Canadian TIS. The authors conclude that this survey was the first to document TIS operations in North America and demonstrates a spectrum of clinical and research activities. It also provides data for a future cost-benefit analysis of TIS.

***Increased frequency of isolated cleft palate in infants exposed to lamotrigine during pregnancy***

***Holmes LB, Baldwin EJ, Smith CR, et al  
Neurology, 2008; Apr 30 [Epub ahead of print]***

Pregnancy registries for women taking anticonvulsant drugs have been developed to more efficiently determine the fetal risks of each drug. This study examined infants with major malformations born to the 791 women who had taken lamotrigine as monotherapy and were enrolled in the North American AED Pregnancy Registry. The medical records were obtained from the affected infants' doctors. Holmes and colleagues conclude that the infant exposed in the first trimester of pregnancy to the anticonvulsant drug lamotrigine has an increased risk to have an isolated cleft palate or cleft lip deformity.

***Methadone maintenance and long-term lactation***

***Breastfeed Med, 2008; 3(1): 34-7  
Jansson LM, Choo R, Velez ML, et al***

The purpose of this research was to examine concentrations of methadone in the plasma and breastmilk of women who breastfeed their infants beyond the neonatal period. Four methadone-maintained women provided blood and breastmilk samples up to six months postpartum. The concentrations of methadone in blood and breastmilk were low, contributing to the recommendation of breastfeeding for some methadone-maintained women.

***Maternal use of loperamide in early pregnancy and delivery outcome***

***Källén B, Nilsson E, Otterblad OP  
Acta Paediatr, 2008; 97(5): 541-5***

The aim of this study was to examine the delivery outcome including the presence of infant congenital malformations after maternal use of loperamide in early pregnancy. Källén and

colleagues conclude that the maternal use of loperamide in early pregnancy may be associated with a moderate risk increase for a malformation in the infant.

***Developments in the pharmacotherapeutic management of spontaneous preterm labor***  
***Kam KYR, Lamont RF***  
***Expert Opin Pharmacother, 2008; 9(7): 1153-68***

The aim of this study was to establish the importance of preterm birth and the huge healthcare costs involved as well as to review the pathophysiology of preterm labor and the use of antepartum glucocorticoids, which are the main reason why tocolytics are used to prevent or delay preterm birth. This study also reviews the range of tocolytics available, their mode of action and the evidence for their efficacy and fetomaternal safety. Kam and Lamont conclude that the perfect tocolytic does not exist. The evidence to support the use of magnesium sulfate as a tocolytic is poor. The use of beta-agonists is decreasing worldwide as clinicians move to nifedipine or atosiban, which are as effective but much safer. Although nifedipine is cheaper than atosiban and can be administered orally, the evidence to support atosiban is much superior to that of nifedipine and there have been recent safety concerns over nifedipine.

***Salivary progesterone and estriol among pregnant women treated with 17-alpha-hydroxyprogesterone caproate or placebo***  
***Klebanoff MA, Meis PJ, Dombrowski MP, et al***  
***Am J Obstet Gynecol, 2008; May 2 [Epub ahead of print]***

The objectives of this study were to determine whether salivary progesterone (P) or estriol (E3) concentration at 16-20 weeks' gestation predicts preterm birth or the response to 17alpha-hydroxyprogesterone caproate (17OHP) and whether 17OHP treatment affected the trajectory of salivary P and E3 as pregnancy progressed. The researchers conclude that 17OHP flattened the trajectory of E3 in the second half of pregnancy, suggesting that the drug influences the fetoplacental unit.

***MotherNature: Establishing a Canadian research network for natural health products (NHPs) during pregnancy and lactation***  
***Koren G, Dugoua JJ, Matsui D, Bérard A, et al***  
***J Altern Complement Med, 2008; May 8 [Epub ahead of print]***

The objective of this study was to create a network for research on natural health products (NHPs) during pregnancy and lactation by forming longstanding collaborations among Canadian medical and complementary and alternative medicine (CAM) practitioners and scientists. MotherNature Network members participated in three 2-day workshops and three conference calls throughout the length of this study. Each member was responsible to lead discussions surrounding one theme and address the following: initiation; development; presentation; and synthesis of comments of all members on the designated theme. As a result, the members were able to prioritize areas in high need for future research and collaborative means to conduct such research. NHPs were prioritized for their importance for future study. Areas for the prospective collection of data on NHP use in pregnancy and lactation were identified. A research and business plan was developed for the long-term sustainability of the Network. Koren and colleagues conclude that the MotherNature Network is well-situated to create a new climate in Canada, where data are collected and interpreted on the effects and safety of NHPs during pregnancy and lactation.

***Safety of dermatologic drugs used in pregnant patients with psoriasis and other inflammatory skin diseases***

***Lam F, Polifka JE, Dohil MA***

***J Am Acad Dermatol, 2008; Apr 12 [Epub ahead of print]***

In patients with psoriasis, there is an increased availability of drugs for treatment. However, there are important questions with regards to drug safety for mothers with psoriasis and their fetuses. Currently, there is limited safety data for many of the medications used. In this article, Lam and colleagues review current pregnancy risk information for medications commonly used in the treatment of psoriasis. In addition, a list of teratology information resources is included to help practicing clinicians find up-to-date information regarding the safety of the medications they prescribe.

***Depression status as a confounder in the effects of antidepressants on the gestation age***

***Lan TH, Wu BJ, Chiu HJ, et al***

***Am J Psychiatry, 2008; 165(3): 399–400; author reply 400***

No abstract available.

***Transfer of chloroquine and desethylchloroquine across the placenta and into milk in Melanesian mothers***

***Law I, Ilett KF, Hackett LP, et al***

***Br J Clin Pharmacol, 2008; 65(5): 674-9***

The objective of this study was to investigate the transfer of chloroquine (CQ) and its major bioactive metabolite desethylchloroquine (DECQ) across the placenta and into breast milk. Law and colleagues conclude that infant exposure to CQ and DECQ during pregnancy will be similar to that in the maternal circulation, and dependent on maternal dose and frequency. The median CQ + DECQ relative infant dose of 3.2% (as CQ equivalents) was low, confirming that use of CQ during lactation is compatible with breastfeeding.

***Changes in enoxaparin pharmacokinetics during pregnancy and implications for antithrombotic therapeutic strategy***

***Lebaudy C, Hulot J, Amoura Z, et al***

***Clin Pharmacol Ther, 2008; Apr 23 [Epub ahead of print]***

Enoxaparin is frequently prescribed for pregnant women who are at high risk for thromboembolic complications. Lebaudy and colleagues conducted a population pharmacokinetics study with 75 pregnant women and 38 nonpregnant women as controls to evaluate enoxaparin pharmacokinetics during pregnancy and the postpartum period. Results revealed that clearance of the drug was higher in the pregnant women throughout pregnancy when compared with nonpregnant women with the stage of the pregnancy having no influence. The volume of distribution was influenced by stage of the pregnancy, characterized by a two-step increase, with an initial rise paralleling the woman's increase in body weight during the first two trimesters, followed by an additional increase of 41% during the last 2 months of pregnancy, independent of changes in weight. Using enoxaparin pharmacokinetic parameters to simulate anti-Xa time profiles, the researchers observed that the maintenance of the same doses throughout pregnancy resulted in a progressive reduction in mean and peak anti-Xa activities. Lebaudy and colleagues recommend the administration of doses normalized for body weight changes so as to counteract enoxaparin pharmacokinetic changes that accompany various stages of pregnancy.

***Maternal asthma medication use and the risk of gastroschisis***

***Lin S, Munsie JP, Herdt-Losavio ML, et al***

***Am J Epidemiol, 2008; Apr 23 [Epub ahead of print]***

The objective of this study was to examine the association between maternal asthma medication use during the periconceptional period and the risk of gastroschisis. In this case-control study, the authors used data on deliveries enrolled in the National Birth Defects Prevention Study (1997-2002) from eight collaborating centers. The cases included 381 infants with isolated gastroschisis, and the controls were 4,121 liveborn infants without malformations. The asthma medications used during the periconceptional period (1 month prepregnancy through the third pregnancy month) were divided into two groups, anti-inflammatory and bronchodilator, and analyzed separately. Users of multiple asthma medications during the periconceptional period were also examined. The researchers conclude that no significant association was found between maternal use of asthma anti-inflammatory medications and gastroschisis. Because information on maternal asthma status/severity was not available, the effects of disease on the risk of gastroschisis cannot be ruled out. Additional research is needed in determining whether a real risk exists and for guiding asthma treatment.

***Methadone maintenance and breastfeeding in the neonatal period***

***Liu AJ, Nanan R***

***Pediatrics, 2008; 121(4): 869; author reply 869-70***

No abstract available.

***Pulmonary tuberculosis in a young pregnant female: challenged in diagnosis and management***

***Maddineni M, Panda M***

***Infect Dis Obstet Gynecol, 2008; Article ID#628985***

Maddineni and Panda describe the case of a 21-year-old Hispanic female presented in preterm labor that was found to be hypoxic. A chest X-ray revealed a paratracheal mass which a CT scan confirmed the PPD test was positive. Bronchoalveolar lavage did not reveal acid-fast bacilli and the biopsy revealed caseating granulomas. Diagnosis and treatment in this case were found to be challenging due to constraints in radiological investigations, lack of initial evidence of acid-fast bacilli, and toxic profile of medications. Due to her high risk, she was started on an antituberculosis regimen. The diagnosis was confirmed on Day 26 when Mycobacterium tuberculosis was isolated by DNA probe. The authors conclude that a high index of suspicion is required to recognize the changing face and disease spectrum of tuberculosis and initiate treatment for better outcomes.

***Twin pregnancy in a patient of chronic myeloid leukemia on imatinib therapy***

***Meera V, Jijina F, Shrikande M, et al***

***Leuk Res, 2008; Apr 15 [Epub ahead of print]***

Imatinib is a tyrosine kinase inhibitor and is now used regularly in chronic myeloid leukaemia therapy in chronic phase with great success. Due to its very nature of action, imatinib is suspected to be teratogenic hence patients are counseled not to get pregnant while on the drug. However, in world literature a few normal pregnancies - though no twin pregnancies - have been reported in patients on imatinib therapy. In this study, Meera and colleagues report the birth of normal mono-ovular mono-chorionic twin while the patient was on imatinib during conception and early pregnancy for chronic myeloid leukaemia.

***Balancing risks: dosing strategies for antidepressants near the end of pregnancy***  
***Miller LJ, Bishop JR, Fischer JH, et al***  
***J Clin Psychiatry, 2008; 69(2): 323-4***

No abstract available.

***Nevirapine concentrations in newborns receiving an extended prophylactic regimen***  
***Mirochnick M, Nielsen SK, Pilotto JH, et al***  
***J Acquir Immune Defic Syndr, 2008; 47(3): 334-7***

The optimal neonatal antiretroviral (ARV) regimen for prevention of HIV mother-to-child transmission (MTCT) is unknown for infants born to mothers who receive no ARVs during pregnancy. As part of a protocol comparing the efficacy of 3 neonatal ARV regimens in preventing HIV-1 MTCT in neonates born to mothers who receive no prenatal treatment with ARVs, the researchers devised a 3-dose nevirapine (NVP) regimen with the goal of maintaining the NVP plasma concentration >100 ng/mL (10 times the in vitro median inhibitory concentration of 10 ng/mL) during the first 2 weeks of life. NVP concentrations were measured in 14 newborns participating in a pharmacokinetics substudy during the second week of life and in single samples from 30 more newborns on day 10 to 14. Results showed that the median NVP elimination half-life was 30.2 hours (range: 17.8 to 50.3 hours). The NVP concentration remained greater than the target of 100 ng/mL in all samples collected through day 10 of life. By day 14, more than half of the newborns in the pharmacokinetic substudy had NVP levels <100 ng/mL, although only 1 neonate had no detectable NVP. Mirochnick and colleagues conclude that although this regimen failed to meet their 100-ng/mL target, it did maintain detectable NVP concentrations in nearly all newborns through the end of the second week of life and is to be used in the parent efficacy protocol

***Birth weight of infants after maternal exposure to typical and atypical antipsychotics: prospective comparison study***  
***Newham JJ, Thomas SH, Macritchie K, et al***  
***Br J Psychiatry 2008; 192: 333-7***

The aim of this study was to determine whether atypical and typical antipsychotics differ in their effects on birth weight after maternal exposure during pregnancy. The researchers found that in utero exposure to atypical antipsychotic drugs may increase infant birth weight and risk of LGA (large for gestational age).

***Maternal depression and medication exposure during pregnancy: comparison of maternal retrospective recall to prospective documentation***  
***Newport DJ, Brennan PA, Green P, et al***  
***BJOG, 2008; 115(6): 681-8***

Outcome investigations of prenatal maternal depression and psychotropic exposure rely extensively on maternal retrospective recall. This study compared postnatal recall to prospective documentation of illness and medication exposures. The results revealed that there was only moderate agreement ( $k = 0.42$ ) in prospective versus retrospective reporting of prenatal depression. Positive predictive value for recalling depression was 90.4%; however, negative predictive value for denying depression was only 53.8%. Participants accurately recalled psychotropic use but significantly underreported use of nonpsychotropic medications. Newport and colleagues conclude that studies using retrospective data collection may be susceptible to

systematic recall bias with underreporting of maternal depression and use of nonpsychotropic agents during pregnancy.

***Local injection of dexamethasone for the treatment of carpal tunnel syndrome in pregnancy***  
***Niempoog S, Sanguanjit P, Waitayawinyu T, et al***  
***J Med Assoc Thai, 2007; 90(12): 2669-76***

The objective of this study was to evaluate the results of 4 mg of dexamethasone acetate injections for the treatment of carpal tunnel syndrome in pregnancy. The authors conclude that carpal tunnel syndrome in pregnancy is generally resolved after delivery and, therefore, should be treated conservatively. The patient with severe symptoms can be treated with dexamethasone injection in the third trimester with good results.

***Maternal use of fluconazole and risk of congenital malformations: a Danish population-based cohort study***  
***Nørgaard M, Pedersen L, Gislum M, et al***  
***J Antimicrob Chemother, 2008; Apr 9 [Epub ahead of print]***

Fluconazole is widely used for the treatment of candidiasis. Although the drug is also prescribed to pregnant women, data on the safety of use of fluconazole during pregnancy are limited. This study examined the association between the maternal use of fluconazole during pregnancy and the risk of congenital malformations. Nørgaard and colleagues conclude that no overall increased risk of congenital malformations was found after exposure to short-course treatment with fluconazole in early pregnancy.

***Review article: use of antitumour necrosis factor therapy in inflammatory bowel disease during pregnancy and conception***  
***O'Donnell S, O'Morain C***  
***Aliment Pharmacol Ther, 2008; 27(1): 885-94***

The aim of this study was to review available data regarding the safety of biological therapies during pregnancy, primarily in women with inflammatory bowel disease. O'Donnell and O'Morain found that based on available data, biological therapies appear to be safe in pregnancy. Most studies looking at the effects of any one medication on pregnancy in inflammatory bowel disease are confounded by the fact that most patients are on multiple medications and have varying levels of disease activity. The cessation of therapy in the third trimester should also be considered. The authors conclude that large registries with longer follow-up periods will be necessary before firm conclusions about the safety of antitumour necrosis factor-alpha therapies during conception and pregnancy can be drawn.

***The outcome of pregnancy following topiramate treatment: A study on 52 pregnancies***  
***Ornoy A, Zvi N, Arnon J, et al***  
***Reprod Toxicol, 2008; Mar 16 [Epub ahead of print]***

In spite of a substantial increase in the use of topiramate at child bearing age, very little is known regarding its use in pregnancy. Ornoy and colleagues describe the outcome of 52 pregnancies with 41 liveborn infants from whom it seems that topiramate reduces birth weight without decreasing gestational age at delivery, but does not seem to increase the risk for structural defects. There was an increased rate of spontaneous abortions; however, this was not related to the drug effects.

***Drugs and breastfeeding: some facts to consider before deciding they are incompatible***

***[Article in French]***

***Panchaud A, Fischer C, Rothuizen L, et al***

***Rev Med Suisse, 2008; 4(146): 540-5***

An increase in the prevalence and duration of breastfeeding has been observed over the last few years in response to promotion campaigns. When a medicamentous treatment is started, discontinuation of breastfeeding is often proposed, for fear of harmful consequences for the infant. Nevertheless such a decision is not unimportant, and it appears that many drugs can actually be used during breastfeeding without significant risk. An assessment of the real risk incurred by exposed children makes it possible to avoid unnecessary discontinuations of breastfeeding. This article aims to review the facts needed to assess amount of drug exposure to the child and to list the few drugs associated with significant effects on the nursing infant.

***Prescribing in pregnancy***

***Paton C***

***Br J Psychiatry, 2008; 192(May): 321-2***

Psychotropic drugs reduce morbidity and mortality related to maternal mental illness but may also cause harm to the foetus, the nature and magnitude of which is not completely understood. According to the author, up-to-date information should be shared as fully as possible with the pregnant woman and a treatment plan agreed jointly.

***Prescription of rimonabant in the early stage of pregnancy?***

***[Article in German]***

***Picksak G, Stichtenoth DO***

***Med Monatsschr Pharm, 2008; 31(3): 107-8***

According to the authors, rimonabant should not be prescribed during pregnancy due to the lack of sufficient data on the teratogenic/embryotoxic risk. A preventive termination of pregnancy is also not indicated. Picksak and Stichtenoth also suggest that women in childbearing years should take only low-risk drugs.

***Pregnancy outcome in women with inflammatory bowel disease following exposure to 5-aminosalicylic acid drugs: a meta-analysis***

***Rahimi R, Nikfar S, Rezaie A, et al***

***Reprod Toxicol, 2008; 25(2): 271-5***

The objective of this study was to explore the risk of adverse pregnancy outcomes in women with IBD following exposure to 5-ASA drugs (mesalazine, sulfasalazine, balsalazide, and olsalazine). Bibliographic databases were searched up to June 2007 for studies investigating pregnancy outcomes in women with IBD following exposure to any 5-ASA drugs. The outcomes of interest were congenital abnormalities, stillbirth, spontaneous abortion, preterm delivery, and low birth weight. Rahimi and colleagues conclude that their meta-analysis suggests that there is no more than an 1.16-fold increase in congenital malformations, an 2.38-fold increase in stillbirth, an 1.14-fold increase in spontaneous abortion, an 1.35-fold increase in preterm delivery, and an 0.93-fold increase in low birth weight.

***Duration of antidepressant use during pregnancy and risk of major congenital malformations***

***Ramos E, St-Andrè M, Rey E, et al***

***Br J Psychiatry, 2008; 192(May): 344-50***

The objective of this study was to determine whether duration of antidepressant use during the first trimester increases the risk of major congenital malformations in offspring of women diagnosed with psychiatric disorders. Ramos and colleagues conclude that these data do not support an association between duration of antidepressant use during the first trimester of pregnancy and major congenital malformations in the offspring of women with psychiatric disorders. These findings should help clinicians decide whether to continue antidepressant therapy during pregnancy.

***Pregnancy and epilepsy: Retrospective analysis of 118 patients***

***[Article in German]***

***Rück J, Bauer J***

***Nervenarzt, 2008; Apr 4 [Epub ahead of print]***

The aim of this study was to evaluate the treatment of women with epilepsy investigated prior to or during pregnancy. Of the study patients, sixty-nine were seen prior to pregnancy, forty-one were on monotherapy with antiepileptic drugs (AED), and twenty-two were already on folic acid supplementation. A change in AED medication was recommended in fifty patients. Ninety-three of the patients were seen during pregnancy, most often during the first trimester. Fifty-one were on AED monotherapy, most often with lamotrigine or valproate. During pregnancy, seizure frequency increased in thirty-three women and decreased in fourteen. The authors conclude that monotherapy with AED should be established if possible, and folic acid supplementation should be started prior to pregnancy.

***Severe facial clefts in acrofacial dysostosis: a consequence of prenatal exposure to mycophenolate mofetil?***

***Schoner K, Steinhard J, Figiel J, et al***

***Obstet Gynecol, 2008; 111(2 Pt. 2): 483-6***

In their study, Schoner and colleagues present a chromosomally normal fetus with severe acrofacial dysostosis and orofacial clefts. These were bilateral transverse and oblique clefts and defects of the midface. In addition, there were preaxial limb anomalies with digitalization of thumbs and internal cardiovascular, gastrointestinal, and urogenital malformations. The mother had been treated with high doses of the immunosuppressant mycophenolate mofetil in early pregnancy for systemic lupus erythematosus. The researchers conclude that mycophenolate mofetil may have contributed to or even caused acrofacial dysostosis phenotype and extensive clefting.

***Secondary effects of antipsychotics: women at greater risk than men***

***Seeman MV***

***Schizophr Bull, 2008; Apr 9 [Epub ahead of print]***

The health burden of antipsychotic medication is well known, but the disproportionate effect on women as compared with men is underappreciated. The goal of this article was preventive - to better inform clinicians so that the risks to women and to their offspring can be diminished. After reviewing all PubMed sources in which the search term gender (or sex) was linked to a side effect of antipsychotic medication, they found general agreement in the literature on women's increased susceptibility to weight gain, diabetes, and specific cardiovascular risks of antipsychotics, with less consensus on malignancy risks and risks to the fetus. Cardiovascular death, to which men are more susceptible than women, is disproportionately increased in women by the use of antipsychotics. Sedating antipsychotics raise the risk of embolic phenomena during

pregnancy, and postpartum. Prolactin-elevating drugs suppress gonadal hormone secretion and may enhance autoimmune proclivity. Seeman concludes that clinicians need to be aware of the differential harm that women (and their offspring) can incur from the side effects of antipsychotics.

***PGE1 nebulisation during caesarean section for Eisenmenger's syndrome: a case report***

***Siddiqui S, Latif N***

***J Med Case Reports, 2008; 2(1): 149 [Epub ahead of print]***

Siddiqui and Latif describe a case of the obstetric anaesthesia management of a 34-year-old, 34-weeks pregnant woman who presented with a recent diagnosis of severe Eisenmenger's syndrome. A combined spinal epidural anaesthesia was used together with invasive cardiac monitoring as well as PGE1 nebulisation after delivery of the baby. This helped to achieve a reduction of shunt, improvement of hypoxia, and reduction of pulmonary pressures.

***Changes in antidepressant metabolism and dosing across pregnancy and early postpartum***

***Sit DK, Perel JM, Helsel JC, et al***

***J Clin Psychiatry; 2008; Mar 11:e1-e7. [Epub ahead of print]***

In this study, Sit and colleagues examined the dose requirements and level-to-dose (L/D) ratios of citalopram, escitalopram, and sertraline during pregnancy and after birth. They found that dose requirements frequently increased during the second half of pregnancy to offset increased drug turnover and maintain optimal pharmacotherapy. These findings replicate and extend earlier published data with other antidepressants.

***Clinical efficacy of antihypertensive therapy of pregnant women with arterial hypertension with long acting nifedipine and bisoprolol***

***[Article in Russian]***

***Striuk RI, Brytkova IaV, Bukhonkina IuM, et al***

***Kardiologiia, 2008; 48(4): 29-33***

The aim of this study was to assess the clinical efficacy of mono therapy with nifedipine SR/GITS and the combination of nifedipine SR/GITS and bisoprolol as well as to investigate of the functional state of sympathoadrenal system (SAS) in pregnant women with arterial hypertension. Examination and treatment with nifedipine SR/GITS 30 mg/day and bisoprolol 2,5 - 5 mg/day was carried out in 21 patients with stage II hypertensive disease (HD) during trimester II of pregnancy. Initially all women including 20 practically healthy pregnant women (control group) had elevation of functional activity of SAS what was determined by high values of b-adrenoception of membranes of erythrocytes. In patients with stage II HD this parameter significantly exceeded that of control group. Administration of antihypertensive drugs for 3 weeks promoted significant lowering of all parameters of 24 hour blood pressure monitoring down to optimal level, lessening of pathological types of 24 hour blood pressure profile and lowering of functional activity of SAS.

***Maternal n-3, n-6, and trans fatty acid profile early in pregnancy and term birth weight: a prospective cohort study***

***van Eijsden M, Hornstra G, van der Wal MF***

***Am J Clin Nutr, 2008; 87(4): 887-95***

The objective of this study was to investigate the association between maternal n-3, n-6, and trans fatty acids measured early in pregnancy and fetal growth. The researchers conclude that an

adverse maternal fatty acid profile early in pregnancy is associated with reduced fetal growth, which, if confirmed, gives perspective for the dietary prevention of lower birth weight.

***Drug management of fetal tachyarrhythmias: are we ready for a systematic and evidence-based approach?***

***van den Heuvel F, Bink-Boelkens MT, du Marchie Sarvaas GJ, et al  
Pacing Clin Electrophysiol, 2008; 31 Suppl 1: S54-7***

Fetal tachyarrhythmias are a life-threatening condition complicating a small proportion of normal pregnancies. Despite major advances in the (intrauterine) pharmacologic treatment of these arrhythmias over the last years major uncertainties remain. Among these are controversies in the choice of agents in relation to arrhythmia type, and timing and duration of treatment. Currently, no evidence-based approach to the management of fetal tachyarrhythmias is available. An international registry is proposed as an important step toward obtaining the necessary data to develop evidence-based management strategies.

***Neonatal transient respiratory depression after maternal urapidil infusion for hypertension***

***Vanhaesebrouck S, Hanssens M, Allegaert K  
Eur J Pediatr, 2008; May 7 [Epub ahead of print]***

Urapidil has been proven to be an effective and well-tolerated antihypertensive drug during pregnancy, but clinical experiences with the drug have been described in only a limited number of studies. In this study, a case of postnatal transient respiratory depression following maternal administration of urapidil is described. The researchers suggest that the fetal and neonatal effects of more recently implemented antihypertensive drugs, such as urapidil, should be included in a prospective evaluation of antihypertensive treatment of women during pregnancy. Infants of mothers who received urapidil should be carefully watched in the immediate postnatal phase as urapidil may still exert some significant effects on the neonate

## LAY PRESS NEWS

***FDA warns mothers about nipple creams***

***CTV.ca, 2008; May 26***

The U.S. Food and Drug Administration have warned mothers not to use or purchase Mommy's Bliss Nipple Cream (marketed by MOM Enterprises Inc. of San Rafeal, California) as it may cause respiratory distress, vomiting, and diarrhea in infants. The cream is promoted to nursing mothers to help soothe dry or cracked nipples. According to the FDA, the cream contains chlorphenesin and phenoxyethanol which may interact with one another to further compound and increase the risk of respiratory depression in nursing infants. Mothers whose children may have suffered adverse effects because of this product are advised to contact the FDA's MedWatch at 1-800-332-1088.

***Antidepressants not linked to birth defects: study***

***CTV.ca, 2008; May 22***

A pregnant woman who takes an antidepressant for any length of time during her first trimester does not increase her chance of delivering a baby with a birth defect, a new Canadian study shows. The study, conducted by researchers from the Universite de Montreal and the Centre Hospitalier Universitaire Saint-Justine, was published Thursday in *The British Journal of*

*Psychiatry*. The researchers analyzed data from more than 2,300 pregnant women in Quebec. The women had been diagnosed with at least one psychiatric disorder before pregnancy and had taken antidepressants for at least 30 days in the year leading up to pregnancy. The research team found no increased risk of delivering a baby with birth defects if a mother took antidepressants during the first 30, 60 or 90 days of her pregnancy. "No statistically significant association was found between antidepressant duration during the first trimester of pregnancy and the risk of major congenital malformations in infants," the study's authors wrote. "In addition, the class of antidepressant used was not significantly associated with the occurrence of major birth defects." The authors also found no difference in birth defect rates between women who used antidepressants during the first trimester and women who had not taken antidepressants at all during pregnancy.

***FDA stresses birth defect risks with Roche drug***  
***Perrone M***  
***MSNBC.com, 2008; May 16***

Health regulators have warned again that Roche and Novartis drugs prescribed to organ transplant patients can cause miscarriages and birth defects when used by pregnant women. Last October, the FDA said it received reports of miscarriages and infants born with ear and mouth birth defects after their mothers took Roche's CellCept. At the time, FDA added its most serious warning to CellCept and a similar Novartis AG drug, Myfortic. FDA spokesman Christopher Kelly said the agency has not received any new reports of pregnancy-related problems, but was concerned some doctors may not have seen the initial warning. CellCept and Myfortic are used to suppress the body's immune system to avoid organ rejection in transplant patients. In a notice posted online Friday, FDA said that before prescribing the drugs doctors should confirm their transplant patients are not pregnant, and are using effective contraception. FDA said most of the reported problems came from mothers who were taking CellCept before their pregnancies were detected. Some of the patients were taking the drug for conditions it was not approved to treat - including rheumatoid arthritis and lupus. A spokesman for Roche said it has not received any new reports of miscarriages or birth defects since updating the drug's labeling. The company previously reported 25 miscarriages among 77 women exposed to the drug between 1995 and 2007.

***Asthma drugs help to prevent birth defects: keep taking medication, women advised***  
***Alphonso C***  
***The Globe and Mail, 2008; May 8: p.A5***

Women who have an asthma attack during the first three months of pregnancy put their babies at a greater risk of birth defects than asthmatic mothers who did not have a flare-up during that period, a new Canadian study shows. The research, published in next month's issue of the *Journal of Allergy and Clinical Immunology* found that women who had uncontrolled asthma during this crucial period in fetal development were 48% more likely to have a baby with at least one birth defect compared with those who were taking their medication. The researchers found that the rate of birth defects a month after the children whose mothers had an asthma exacerbation was 12.8%, compared to 8.9% for pregnant women with controlled asthma during the first trimester. The rate of birth defects in the general population is anywhere from 3% to 6%. The most frequent birth defects reported were musculoskeletal and cardiac. Lead author of the study, Professor Lucie Blais said, "I hope it will encourage women to continue their treatment during pregnancy. This gives some evidence that stopping your treatment and then being more at risk of having an asthma attack puts your baby at risk of having a congenital malformation." Birth defects can be more common due to the drop in the level of oxygen in the blood of both the fetus and the mother

when the pregnant woman has difficulty breathing. A baby needs a consistent supply of blood for normal growth and survival. "If you take moderate doses of inhaled corticosteroids, which is the medication they would take to control their asthma...this will reduce the risk of having an asthma attack and then reduce the risk of having a malformation," Professor Blais said. "They should take their medication as prescribed, as usual."

***Pill effective against pregnancy-related diabetes***

***Emery G***

***Reuters News, 2008; May 7***

According to researchers in New Zealand and Australia, The diabetes pill metformin is just as effective as insulin injections in treating women who develop diabetes during pregnancy. So-called gestational diabetes surfaces in one out of every 20 pregnant women, and there has been concern that metformin might affect a fetus because the drug can cross the placenta. But the study, led by Janet Rowan of the Auckland City Hospital in New Zealand, found that the risk of complications such as respiratory distress, birth trauma and newborn hypoglycemia, or low blood sugar, was no different for the 363 women who received metformin and the 370 given conventional insulin shots. Metformin is available generically but also known by the Bristol-Myers Squibb brand name Glucophage. After delivery, nearly 77 percent of the metformin recipients said they would want to stay with the pill if they developed diabetes during pregnancy again, even though 46 percent still needed supplemental insulin injections at some point. Only 27 percent of those who got insulin shots felt the same way, they reported in the New England Journal of Medicine. But doctors may still be cautious, the researchers said. "Clinicians may remain circumspect about using metformin until follow-up data for offspring are available," they wrote. The children born during the study are being tested when they reach their second birthday.

***Paracetamol may increase asthma risk***

***Daily Mail, 2008; April 28***

Research shows that children whose mothers used paracetamol during the first three months of pregnancy had a 45 per cent increased risk of asthma by age seven. The international team of specialists who carried out the research believes the guidelines on use of the drug may need to be reconsidered. Researchers found that paracetamol use at any time during pregnancy was associated with a 17 per cent increased risk of asthma and bronchitis at 18 months and a 15 per cent increased risk of asthma at the age of seven. One theory is that paracetamol lowers the body's defenses by reducing levels of glutathione, an antioxidant found naturally in the airways. It is believed that glutathione reduces inflammation during an asthma attack.