

# Obstetrics

## Evidence Update

### July 2017 (Bimonthly)



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# Training Calendar 2017

*All sessions are one hour*

## July (13.00-14.00)

3rd (Mon) Interpreting Statistics  
12th (Wed) Critical Appraisal  
21st (Fri) Literature Searching  
26th (Wed) Interpreting Statistics

## August (12.00-13.00)

4th (Fri) Critical Appraisal  
9th (Wed) Literature Searching  
15th (Tues) Interpreting Statistics  
24th (Thurs) Critical Appraisal

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# The Latest Evidence

**NICE** National Institute for  
Health and Care Excellence

## In development

[Cervical ripening balloon for the induction of labour in women who have previously undergone cesarean section \(GID-IP1131\)](#) <sup>TBC</sup> **Interventional procedures guidance**

[Intrapartum care for high risk women \(GID-CGWAVE0613\)](#) March 2019 **NICE guidelines**

[PartoSure \(and alternative technologies identified during scoping\) to help predict preterm labour in women with intact membranes \(GID-DG10017\)](#) July 2018 **Diagnostics guidance**

[Developmental follow-up of children and young people born preterm \(GID-CGWAVE0752\)](#)

August 2017 **NICE guidelines**

[Developmental follow-up of pre-term babies \(GID-QS10053\)](#) May 2018 **Quality standards**

[Postnatal care up to 8 weeks after birth \(update\) \(GID-NG10070\)](#) January 2020 **NICE guidelines**

[Specialist neonatal respiratory care for babies born preterm \(GID-NG10039\)](#) April 2019 **NICE guidelines**



[Continuous support for women during childbirth](#)

Meghan A Bohren, G Justus Hofmeyr, Carol Sakala, Rieko K Fukuzawa, Anna Cuthbert

[Exercise for pregnant women with gestational diabetes for improving maternal and fetal outcomes](#)

Julie Brown, Gilles Ceysens, Michel Boulvain

[Fetal and umbilical Doppler ultrasound in high-risk pregnancies](#)

Zarko Alfirovic, Tamara Stampalija, Therese Dowswell

[Perineal techniques during the second stage of labour for reducing perineal trauma](#)

Vigdis Aasheim, Anne Britt Vika Nilsen, Liv Merete Reinart, Mirjam Lukasse

[Treating periodontal disease for preventing adverse birth outcomes in pregnant women](#)

Zipporah Ihezor-Ejiofor, Philippa Middleton, Marco Esposito, Anne-Marie Glenny

A systematic review of studies assessing an intervention for a health problem.

[Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes](#)

Foong Ming Moy, Amita Ray, Brian S Buckley, Helen M West

[Methods of term labour induction for women with a previous caesarean section](#)

Helen M West, Marta Jozwiak, Jodie M Dodd A systematic review of studies assessing an intervention for a health problem.

[Cervical stitch \(cerclage\) for preventing preterm birth in singleton pregnancy](#)

Zarko Alfirovic, Tamara Stampalija, Nancy Medley

[Position in the second stage of labour for women without epidural anaesthesia](#)

Janesh K Gupta, Akanksha Sood, G Justus Hofmeyr, Joshua P Vogel

[Lifestyle interventions for the treatment of women with gestational diabetes](#)

Julie Brown, Nisreen A Alwan, Jane West, Stephen Brown, Christopher JD McKinlay, Diane Farrar, Caroline A Crowther

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## **OBSTETRICS**

### **In utero exposure to beta-blockers and congenital heart disease (June 2017)**

Although several previous studies have suggested an association between in utero exposure to beta-blockers and congenital heart disease, the most recent study found no association after adjusting for maternal age, maternal body mass index, and maternal comorbidities [1]. Further research is required given the limitations of available studies, including inability to analyze data by type of beta-blocker, variability in timing of exposure within the first trimester, differences in indications for beta-blocker therapy, and recall, recording, publication, and survivor biases. When first trimester antihypertensive therapy is indicated, we suggest using either [methyldopa](#) or [labetalol](#). (See "[Management of hypertension in pregnant and postpartum women](#)", section on 'Beta-blockers'.)

### **Neuraxial anesthesia in parturients with thrombocytopenia (June 2017)**

The risk of spinal epidural hematoma (SEH) associated with neuraxial anesthesia (NA) techniques in patients with thrombocytopenia is poorly defined because SEH is rare. In a systematic review of over 1500 NA procedures in parturients with platelet counts less than 100,000 /microL, no cases of epidural hematoma requiring decompressive laminectomy were identified [2]. A statistical analysis based on data from this cohort suggests that the incidence of epidural hematoma may range from 0.2 percent (for platelet counts 70 to 100,000/microL) to 11 percent (for platelet counts <49,000/microL). These estimates may inform clinical decision-making regarding performance of NA in parturients with thrombocytopenia. (See "[Adverse effects of neuraxial analgesia and anesthesia for obstetrics](#)", section on '[Neuraxial analgesia and low platelets](#)'.)

### **IVF-conceived pregnancy and Down syndrome screening (June 2017)**

In vitro fertilization (IVF) (with or without intracytoplasmic sperm injection) can affect maternal serum marker levels to mimic the pattern associated with Down syndrome. In a meta-analysis of studies that compared free  $\beta$ -human chorionic gonadotropin (hCG) levels, pregnancy-associated plasma protein A (PAPP-A) levels, and nuchal translucency measurements in IVF pregnancies with those in spontaneously-conceived pregnancies, PAPP-A was reduced by 15 percent, free beta-hCG was slightly increased, and nuchal translucency was unaffected by IVF [3]. Based on these and other data, we recommend that clinicians inform the laboratory when specimens are taken from patients with IVF-conceived pregnancies, so that the laboratory can make appropriate adjustments in reported multiples of median (MoM), to reduce the need for follow-up invasive testing or secondary cell-free-DNA screening. (See "[Laboratory issues related to maternal serum screening for Down syndrome](#)", section on '[Assisted reproduction techniques](#)'.)

### **Antenatal exposure to lithium and congenital cardiac defects (June 2017)**

Fetal [lithium](#) exposure may increase the risk of cardiac malformations, although the data are conflicting. In a retrospective study examining cardiac defects in infants exposed to lithium or [lamotrigine](#) during the first trimester, cardiac malformations occurred more frequently in infants exposed to lithium (2.4 versus 1.4 percent) [4]. There was a dose-response relationship between the lithium dose and the risk of cardiac malformations. These results support using lamotrigine for euthymic patients with bipolar disorder who are pregnant or planning a pregnancy and are receiving maintenance pharmacotherapy. (See "[Teratogenicity, pregnancy complications, and postnatal risks of antipsychotics, benzodiazepines, lithium, and electroconvulsive therapy](#)", section on '[Cardiac](#)'.)

### **Rising rates of HCV infection in young women in the United States (May 2017)**

In parallel with the opioid and injection drug use epidemic in the United States, rates of

hepatitis C virus (HCV) infection have been increasing over the past decade. In particular, the annual number of acute HCV cases among women aged 15 to 44 years rose 3.6-fold from 2006 to 2014 [5]. An estimated 29,000 women with HCV infection gave birth each year between 2011 and 2014; since the risk of vertical transmission is approximately 5.8 percent, this implies that an estimated 1700 infants were infected annually during this time. These numbers highlight the importance of screening at-risk individuals and arranging follow-up for those with HCV infection. (See "[Vertical transmission of hepatitis C virus](#)", section on '[Incidence](#)' and "[Hepatitis C virus infection in children](#)", section on '[Epidemiology](#)'.)

### **Tranexamic acid for management of postpartum hemorrhage (May 2017)**

[Tranexamic acid](#), an antifibrinolytic drug, reduces bleeding in surgical and trauma patients. In a pragmatic randomized trial involving over 20,000 women with postpartum hemorrhage in over 20 countries (the World Maternal Antifibrinolytic Randomized Trial [WOMAN]), tranexamic acid, compared with placebo, reduced the relative risk of death due to bleeding by 20 to 30 percent, reduced the incidence of laparotomy to control bleeding, and was not associated with an increase in adverse effects [6]. Overall mortality was not reduced. We now recommend administration of tranexamic acid as a component of the treatment for postpartum hemorrhage. (See "[Postpartum hemorrhage: Medical and minimally invasive management](#)".)

### **USPSTF guidelines on screening for preeclampsia (May 2017)**

The US Preventive Services Task Force (USPSTF) affirmed the long-standing practice of screening pregnant women for preeclampsia with blood pressure measurements throughout pregnancy [7]. In contrast to traditional practice, they concluded that evidence does not support point-of-care urine testing to screen for preeclampsia. We suggest testing for proteinuria at the first prenatal visit to establish a baseline and, given the possibility for false-positives and false-negatives, repeating the test in asymptomatic normotensive patients on at least one subsequent prenatal visit. (See "[Preeclampsia: Clinical features and diagnosis](#)", section on '[Screening](#)'.)

### **Maternal Tdap vaccination and prevention of infant pertussis (May 2017)**

Immunization with the tetanus, diphtheria, and acellular pertussis (Tdap) vaccine is recommended for women during each pregnancy in order to provide passive protection against pertussis to their infants. Although passive transfer of maternal antibodies can blunt the infant's own immune response to infant doses of the diphtheria, tetanus toxoids, and acellular pertussis (DTaP) vaccine, it does not appear to interfere with clinical vaccine efficacy. In a retrospective study of nearly 150,000 infants at every level of DTaP vaccine exposure, infants exposed in utero to Tdap vaccine were better protected against pertussis



during the first year of life than infants not exposed in utero [8]. (See "[Immunizations during pregnancy](#)", section on 'Rationale, efficacy, and safety'.)

### **Persistence of neurotoxicity of childhood lead poisoning into adulthood (May 2017)**

Detectable blood lead levels (BLLs) are associated with irreversible neurocognitive deficits in children and a BLL lower limit for this toxicity has **not** been established. Previous studies had shown that this effect persists into adolescence. In a longitudinal cohort study of over 1000 patients, lead exposure, based upon BLLs obtained at 11 years of age, was associated in a dose-dependent fashion with lower intelligence quotient (IQ) and lower socioeconomic status at age 38 years after adjustment for maternal IQ, child IQ, and childhood socioeconomic status [9]. Thus, childhood lead exposure causes neurotoxicity that persists into adulthood. Primary prevention of lead exposure, including in pregnant women, can prevent these effects. (See "[Childhood lead poisoning: Clinical manifestations and diagnosis](#)", section on 'Neurologic'.)

## Journal Tables of Contents

Click on the hyperlinked title (+ Ctrl) for contents. If you would like any of the papers in full then please email the library: [library@uhbristol.nhs.uk](mailto:library@uhbristol.nhs.uk)

Journal	Month	Volume	Issue
<a href="#">Obstetrics and Gynaecology</a>	July 2017	130	1
<a href="#">British Journal of Obstetrics and Gynaecology</a>	July 2017	124	8
<a href="#">American Journal of Obstetrics and Gynecology</a>	July 2017	217	1

## Exercise: Confounding Bias in Research Methodology

*A confounder is a factor that is:*

- *Linked to the outcome of interest, independent of the exposure*
- *Linked to the exposure but not the consequence of the exposure*

**What is the confounding factor in the following relationships:**

- People who carry matches are more likely to develop lung cancer
- People who eat ice-cream are more likely to drown
- Training in anaesthesia is more likely to make doctors commit suicide

*To find out more about bias in research methodology, sign up for one of our **Critical Appraisal training sessions**. For more details, email [library@uhbristol.nhs.uk](mailto:library@uhbristol.nhs.uk).*

## Database Articles

If you require any of the articles in full please email: [library@uhbristol.nhs.uk](mailto:library@uhbristol.nhs.uk)

### 1. Association of prenatal exposure to perfluoroalkyl substances with cord blood adipokines and birth size: The Hokkaido Study on environment and children's health.

**Author(s):** Minatoya, Machiko; Itoh, Sachiko; Miyashita, Chihiro; Araki, Atsuko; Sasaki, Seiko; Miura, Ryu; Goudarzi, Houman; Iwasaki, Yusuke; Kishi, Reiko

**Source:** Environmental research; Jul 2017; vol. 156 ; p. 175-182

**Publication Date:** Jul 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28349882

**Abstract:**Perfluoroalkyl substances (PFASs) are synthetic chemicals that persist in the environment and in humans. There is a possible association between prenatal PFASs exposure and both neonate adipokines and birth size, yet epidemiological studies are very limited. The objective of this study was to examine associations of prenatal exposure to PFASs with cord blood adipokines and birth size. We conducted birth cohort study, the Hokkaido Study. In this study, 168 mother-child pairs were included. Perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in maternal blood were determined by liquid chromatography tandem mass spectrometry. Cord blood adiponectin and leptin levels were measured by ELISA and RIA, respectively. Birth weight and ponderal index (PI) were obtained from birth record. The median maternal PFOS and PFOA were 5.1 and 1.4ng/mL, respectively. The median total adiponectin and leptin levels were 19.4µg/mL and 6.2ng/mL, respectively. Adjusted linear regression analyses found that PFOS level was positively associated with total adiponectin levels ( $\beta=0.12$ , 95% CI:0.01, 0.22), contrary was negatively associated with PI ( $\beta=-2.25$ , 95% CI: -4.01, -0.50). PFOA level was negatively associated with birth weight ( $\beta=-197$ , 95% CI: -391, -3). Leptin levels were not associated with PFASs levels. PFOS and adiponectin levels showed marginal dose-response relationship and both PFOS and PFOA and birth size showed significant dose-response relationships. Results from this study suggested that prenatal PFASs exposure may alter cord blood adiponectin levels and may decrease birth size.

**Database:** Medline

### 2. Utility of multiparametric MRI in Caesarean section scar characterization and preoperative prediction of scar dehiscence: a prospective study.

**Author(s):** Kumar, Ishan; Verma, Ashish; Matah, Manjari; Satpathy, Gayatri

**Source:** Acta radiologica (Stockholm, Sweden : 1987); Jul 2017; vol. 58 (no. 7); p. 890-896

**Publication Date:** Jul 2017

**Publication Type(s):** Journal Article

**PubMedID:** 27799572

**Abstract:**Background Post-Caesarean uterine scar rupture during vaginal birth after Caesarean section (VBAC) is a potentially life-threatening complication. Prediction of scar dehiscence and scar rupture is vital in treatment planning and selecting candidates of trial of labor after a Caesarean section (CS). Purpose To assess the accuracy of magnetic resonance imaging (MRI) for evaluation of post-Caesarean uterine scar and to predict scar dehiscence during repeat CS. Material and Methods Thirty patients with a history of at least one previous CS underwent pelvic MRI for assessment of

uterine scar during a subsequent gestation, all of whom underwent lower segment Caesarean section (LSCS) subsequently due to one of the established indications of CSs. Thickness, T1, T2 signal intensity ratio (SER), and apparent diffusion coefficient (ADC) value of scar site were charted. The lower uterine segment was assessed and graded intraoperatively and findings were correlated with MRI findings. Results A total of 30 participants were included in this study, of which nine were classified as having an abnormal scar (of various grades) based on surgical observations. T2 SER with a cutoff value of 0.935 showed the highest sensitivity of 100% and scar thickness value of 3.45 mm showed highest specificity of 91% in prediction of abnormal scar. On drawing a receiver operating characteristic (ROC) curve, T2 signal intensity ratio showed the highest area under the curve (AUC) closely followed by scar thickness values. Conclusion MRI derived parameters may be utilized for differentiation of an abnormal post-Caesarean uterine scar from a normal one. Both scar thickness and T2 SER measured on MRI can be used to predict scar dehiscence. However, T2 SER can serve as a more standardized and objective criterion.

**Database:** Medline

### **3. Maternal Obesity and Cerebral Palsy in Offspring-Reply.**

**Author(s):** Villamor, Eduardo; Tedroff, Kristina; Cnattingius, Sven

**Source:** JAMA; Jun 2017; vol. 317 (no. 24); p. 2550

**Publication Date:** Jun 2017

**Publication Type(s):** Letter Comment

**PubMedID:** 28655006

Available in full text at [JAMA \[JAMA\] NLMUID: 7501160](#) - from EBSCOhost

**Database:** Medline

### **4. Maternal Obesity and Cerebral Palsy in Offspring.**

**Author(s):** Li, Yong-Jiang; Li, Ya-Min

**Source:** JAMA; Jun 2017; vol. 317 (no. 24); p. 2549-2550

**Publication Date:** Jun 2017

**Publication Type(s):** Letter Comment

**PubMedID:** 28655001

Available in full text at [JAMA \[JAMA\] NLMUID: 7501160](#) - from EBSCOhost

**Database:** Medline

### **5. Risk of major congenital malformations in relation to maternal overweight and obesity severity: cohort study of 1.2 million singletons.**

**Author(s):** Persson, Martina; Cnattingius, Sven; Villamor, Eduardo; Söderling, Jonas; Pasternak, Björn; Stephansson, Olof; Neovius, Martin

**Source:** BMJ (Clinical research ed.); Jun 2017; vol. 357 ; p. j2563

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28615173

Available in full text at [The BMJ](#) - from Highwire Press

**Abstract:**Objective To estimate the risks of major congenital malformations in the offspring of mothers who are underweight (body mass index (BMI) <18.5), overweight (BMI 25 to <30), or in obesity classes I (BMI 30 to <35), II (35 to <40), or III ( $\geq$ 40) compared with offspring of normal weight mothers (BMI 18.5 to <25) in early pregnancy.Design Population based cohort study.Setting Nationwide Swedish registries.Participants 1 243 957 liveborn singleton infants from 2001 to 2014 in Sweden. Data on maternal and pregnancy characteristics were obtained by individual record linkages.Exposure Maternal BMI at the first prenatal visit.Main outcome measures Offspring with any major congenital malformation, and subgroups of organ specific malformations diagnosed during the first year of life. Risk ratios were estimated using generalised linear models adjusted for maternal factors, sex of offspring, and birth year.Results A total of 43 550 (3.5%) offspring had any major congenital malformation, and the most common subgroup was for congenital heart defects (n=20 074; 1.6%). Compared with offspring of normal weight mothers (risk of malformations 3.4%), the proportions and adjusted risk ratios of any major congenital malformation among the offspring of mothers with higher BMI were: overweight, 3.5% and 1.05 (95% confidence interval 1.02 to 1.07); obesity class I, 3.8% and 1.12 (1.08 to 1.15), obesity class II, 4.2% and 1.23 (1.17 to 1.30), and obesity class III, 4.7% and 1.37 (1.26 to 1.49). The risks of congenital heart defects, malformations of the nervous system, and limb defects also progressively increased with BMI from overweight to obesity class III. The largest organ specific relative risks related to maternal overweight and increasing obesity were observed for malformations of the nervous system. Malformations of the genital and digestive systems were also increased in offspring of obese mothers.Conclusions Risks of any major congenital malformation and several subgroups of organ specific malformations progressively increased with maternal overweight and increasing severity of obesity. For women who are planning pregnancy, efforts should be encouraged to reduce adiposity in those with a BMI above the normal range.

**Database:** Medline

## 6. Lithium Use in Pregnancy and the Risk of Cardiac Malformations.

**Author(s):** Patorno, Elisabetta; Huybrechts, Krista F; Bateman, Brian T; Cohen, Jacqueline M; Desai, Rishi J; Mogun, Helen; Cohen, Lee S; Hernandez-Diaz, Sonia

**Source:** The New England journal of medicine; Jun 2017; vol. 376 (no. 23); p. 2245-2254

**Publication Date:** Jun 2017

**Publication Type(s):** Comparative Study Journal Article

**PubMedID:** 28591541

Available in full text at [New England Journal of Medicine](#) - from Ovid

**Abstract:**BACKGROUNDThere has been concern that exposure to lithium early in pregnancy may be associated with a marked increase in the risk of Ebstein's anomaly (a right ventricular outflow tract obstruction defect) in infants and overall congenital cardiac defects, but data are conflicting and limited.METHODSWe conducted a cohort study involving 1,325,563 pregnancies in women who were enrolled in Medicaid and who delivered a live-born infant between 2000 and 2010. We examined the risk of cardiac malformations among infants exposed to lithium during the first trimester as compared with unexposed infants and, in secondary analyses, with infants exposed to another commonly used mood stabilizer, lamotrigine. Risk ratios and 95% confidence intervals were estimated with control for psychiatric and medical conditions, medications, and other potential confounders.RESULTSCardiac malformations were present in 16 of the 663 infants exposed to lithium (2.41%), 15,251 of the 1,322,955 nonexposed infants (1.15%), and 27 of the 1945 infants exposed to lamotrigine (1.39%). The adjusted risk ratio for cardiac malformations among infants exposed to lithium as compared with unexposed infants was 1.65 (95% confidence interval [CI], 1.02 to 2.68). The risk ratio was 1.11 (95% CI, 0.46 to 2.64) for a daily dose of 600 mg or less, 1.60 (95% CI,

0.67 to 3.80) for 601 to 900 mg, and 3.22 (95% CI, 1.47 to 7.02) for more than 900 mg. The prevalence of right ventricular outflow tract obstruction defects was 0.60% among lithium-exposed infants versus 0.18% among unexposed infants (adjusted risk ratio, 2.66; 95% CI, 1.00 to 7.06). Results were similar when lamotrigine-exposed infants were used as the reference group. **CONCLUSIONS** Maternal use of lithium during the first trimester was associated with an increased risk of cardiac malformations, including Ebstein's anomaly; the magnitude of this effect was smaller than had been previously postulated. (Funded by the National Institute of Mental Health.).

**Database:** Medline

## 7. Gestational Weight Gain and Outcomes for Mothers and Infants.

**Author(s):** Caughey, Aaron B

**Source:** JAMA; Jun 2017; vol. 317 (no. 21); p. 2175-2176

**Publication Date:** Jun 2017

**Publication Type(s):** Editorial Comment

**PubMedID:** 28586874

Available in full text at [JAMA \[JAMA\] NLMUID: 7501160](#) - from EBSCOhost

**Database:** Medline

## 8. Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy.

**Author(s):** Rawlinson, William D; Boppana, Suresh B; Fowler, Karen B; Kimberlin, David W; Lazzarotto, Tiziana; Alain, Sophie; Daly, Kate; Doutré, Sara; Gibson, Laura; Giles, Michelle L; Greenlee, Janelle; Hamilton, Stuart T; Harrison, Gail J; Hui, Lisa; Jones, Cheryl A; Palasanthiran, Pamela; Schleiss, Mark R; Shand, Antonia W; van Zuylen, Wendy J

**Source:** The Lancet. Infectious diseases; Jun 2017; vol. 17 (no. 6); p. e177

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article Review

**PubMedID:** 28291720

**Abstract:** Congenital cytomegalovirus is the most frequent, yet under-recognised, infectious cause of newborn malformation in developed countries. Despite its clinical and public health importance, questions remain regarding the best diagnostic methods for identifying maternal and neonatal infection, and regarding optimal prevention and therapeutic strategies for infected mothers and neonates. The absence of guidelines impairs global efforts to decrease the effect of congenital cytomegalovirus. Data in the literature suggest that congenital cytomegalovirus infection remains a research priority, but data are yet to be translated into clinical practice. An informal International Congenital Cytomegalovirus Recommendations Group was convened in 2015 to address these questions and to provide recommendations for prevention, diagnosis, and treatment. On the basis of consensus discussions and a review of the literature, we do not support universal screening of mothers and the routine use of cytomegalovirus immunoglobulin for prophylaxis or treatment of infected mothers. However, treatment guidelines for infected neonates were recommended. Consideration must be given to universal neonatal screening for cytomegalovirus to facilitate early detection and intervention for sensorineural hearing loss and developmental delay, where appropriate. The group agreed that education and prevention strategies for mothers were

beneficial, and that recommendations will need continual updating as further data become available.

**Database:** Medline

### **9. Analysis of Milk from Mothers Who Delivered Prematurely Reveals Few Changes in Proteases and Protease Inhibitors across Gestational Age at Birth and Infant Postnatal Age.**

**Author(s):** Demers-Mathieu, Veronique; Nielsen, Søren Drud; Underwood, Mark A; Borghese, Robyn; Dallas, David C

**Source:** The Journal of nutrition; Jun 2017; vol. 147 (no. 6); p. 1152-1159

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28424255

Available in full text at [Journal of nutrition \[J Nutr\] NLMUID: 0404243, The](#) - from EBSCOhost

**Abstract:**Background: Peptidomics research has demonstrated that protease activity is higher in breast milk from preterm-delivering mothers than from term-delivering mothers. However, to our knowledge, the effect of the degree of prematurity and postnatal age on proteases and protease inhibitors in human milk remains unknown.Objective: We aimed to determine the change of proteases and protease inhibitors in milk from mothers who delivered prematurely across gestational age (GA) and postnatal age.Methods: Milk samples were collected from 18 mothers aged 26-40 y who delivered preterm infants and who lacked mastitis. For analysis, samples were separated into 2 groups: 9 from early GA (EGA) (24-26 wk GA)-delivering mothers and 9 from late GA (LGA) (27-32 wk GA)-delivering mothers. Within the 9 samples in each group, the collection time ranged from postnatal days 2 to 47. The activity and predicted activity of proteases in preterm milk were determined with the use of fluorometric and spectrophotometric assays and peptidomics, respectively. Protease and protease inhibitor concentrations were determined with the use of ELISA. Linear mixed models were applied to compare enzymes across GA and postnatal age.Results: Carboxypeptidase B2, kallikrein, plasmin, elastase, thrombin, and cytosol aminopeptidase were present and active in the milk of preterm-delivering mothers. Most milk protease and antiprotease concentrations did not change with GA or postnatal age. However, the concentration and activity of kallikrein, the most abundant and active protease in preterm milk, increased by 25.4 ng · mL<sup>-1</sup> · d<sup>-1</sup> and 0.454 µg · mL<sup>-1</sup> · d<sup>-1</sup> postnatally, respectively, in EGA milk samples while remaining stable in LGA milk samples.Conclusions: This research demonstrates that proteases are active in human milk and begin to degrade milk protein within the mammary gland before consumption by infants. Proteases and protease inhibitors in milk from mothers of premature infants mostly did not vary substantially across GA and postnatal age.

**Database:** Medline

### **10. Upregulation of Zinc Absorption Matches Increases in Physiologic Requirements for Zinc in Women Consuming High- or Moderate-Phytate Diets during Late Pregnancy and Early Lactation.**

**Author(s):** Hambidge, K Michael; Miller, Leland V; Mazariegos, Manolo; Westcott, Jamie; Solomons, Noel W; Raboy, Victor; Kemp, Jennifer F; Das, Abhik; Goco, Norman; Hartwell, Ty; Wright, Linda; Krebs, Nancy F

**Source:** The Journal of nutrition; Jun 2017; vol. 147 (no. 6); p. 1079-1085

**Publication Date:** Jun 2017

**Publication Type(s):** Randomized Controlled Trial Journal Article



**PubMedID:** 28424260

Available in full text at [Journal of nutrition \[J Nutr\] NLMUID: 0404243, The](#) - from EBSCOhost

**Abstract:**Background: Estimated physiologic requirements (PRs) for zinc increase in late pregnancy and early lactation, but the effect on dietary zinc requirements is uncertain.Objective: The aim of this study was to determine changes in daily fractional absorbed zinc and total absorbed zinc (TAZ) from ad libitum diets of differing phytate contents in relation to physiologic zinc requirements during pregnancy and lactation.Methods: This was a prospective observational study of zinc absorption at 8 (phase 1) and 34 (phase 2) wk of gestation and 2 (phase 3) and 6 (phase 4) mo of lactation. Participants were indigenous Guatemalan women of childbearing age whose major food staple was maize and who had been randomly assigned in a larger study to either of 2 ad libitum feeding groups: low-phytate maize (LP; 1.6 mg/g; n = 14) or control maize (C; 7.1 mg/g; n = 8). Total dietary zinc (milligrams per day, TDZ) and phytate (milligrams per day) were determined from duplicate diets and fractional absorption (FAZ) by dual isotope ratio technique (TAZ = TDZ × FAZ). All variables were examined longitudinally and by group and compared with PRs. TAZ values at later phases were compared with phase 1. Measured TAZ was compared with predicted TAZ for nonpregnant, nonlactating (NPNL) women.Results: TAZ was greater in the LP group than in the C group at all phases. All variables increased from phase 1 to phases 2 and 3 and declined at phase 4. TAZ increased by 1.25 mg/d (P = 0.045) in the C group and by 0.81 mg/d (P = 0.058) in the LP group at phase 2. At phase 3, the increases were 2.66 mg/d (P = 0.002) in the C group and 2.28 mg/d (P = 0.0004) in the LP group, compared with a 1.37-mg/d increase in PR. Measured TAZ was greater than predicted values in phases 2-4.Conclusions: Upregulation of zinc absorption in late pregnancy and early lactation matches increases in PRs of pregnant and lactating women, regardless of dietary phytate, which has implications for dietary zinc requirements of pregnant and lactating women.

**Database:** Medline

### **11. Alterations in Lipid Profile, Zinc and Copper Levels and Superoxide Dismutase Activities in Normal Pregnancy and Preeclampsia.**

**Author(s):** Keshavarz, Pardis; Nobakht M Gh, B Fatemeh; Mirhafez, Seyed Reza; Nematy, Mohsen; Azimi-Nezhad, Mohsen; Afin, Sedigheh Ayati; Esmaily, Habibollah; Pournali, Leila; Hakak, Atieh Mehdizadeh; Soukhtanloo, Mohammad; Mirteimouri, Masoumeh; Ghomian, Nayereh; Ferns, Gordon A

**Source:** The American journal of the medical sciences; Jun 2017; vol. 353 (no. 6); p. 552-558

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28641718

**Abstract:**BACKGROUNDIncreased oxidative stress (OS) and lipid peroxidation may be involved in the pathogenesis of preeclampsia (PE). We conducted a case-control study to evaluate the levels of plasma lipids and trace elements as well as activity of superoxide dismutase (SOD) in PE.MATERIALS AND METHODSThe study consisted of 100 patients who had been diagnosed with PE and 100 normotensive pregnant women who underwent medical checkups that served as the control group. Lipid profile, zinc (Zn) and copper (Cu) levels and SOD activities were measured in the plasma of all subjects.RESULTSOur results showed that the plasma levels of triglycerides and SOD activity were significantly elevated and the levels of Zn and Cu were significantly reduced in patients with PE compared with healthy controls. Increased levels of SOD may indicate antioxidant protective mechanisms against OS in PE-complicated pregnancies. This finding may suggest an involvement of OS in the pathophysiology of PE.CONCLUSIONThis study demonstrated a significant negative correlation between SOD activity and levels of trace elements. Furthermore, we suggest that higher

triglyceride levels and SOD activity combined with lower Zn and Cu levels may be associated with an increased risk of PE.

**Database:** Medline

### **12. CE: Original Research: The Experiences of Pregnant Smokers and Their Providers.**

**Author(s):** Britton, Geraldine Rose; Collier, Rosemary; McKittrick, Sean; Sprague, Lori Marie; Rhodes-Keefe, Joyce; Feeney, Ann; James, Gary D

**Source:** The American journal of nursing; Jun 2017; vol. 117 (no. 6); p. 24-34

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28504975

**Abstract::** Background: The U.S. Department of Health and Human Services' initiative Healthy People 2020 targets tobacco use, including smoking during pregnancy, as a continuing major health concern in this country. Yet bringing the U.S. Public Health Service's 2008 clinical practice guideline, Treating Tobacco Use and Dependence, into routine prenatal care remains challenging. Our previous nurse-managed intervention study of rural pregnant women found no significant cessation effect and significant discordance between self-reported smoker status and urinary cotinine levels. **PURPOSE**The overall purpose of this follow-up study was to increase our understanding of the experiences of pregnant smokers and their providers. No qualitative studies could be found that simultaneously explored the experiences of both groups. **DESIGN AND METHOD**This qualitative descriptive study used focus group methodology. Nine focus groups were held in two counties in upper New York State; six groups consisted of providers and three consisted of pregnant women. Four semistructured questions guided the group discussions, which were audiotaped and transcribed verbatim. Transcripts were read and coded independently by six investigators. Themes were identified using constant comparative analysis and were validated using the consensus process. **RESULT**The total sample consisted of 66 participants: 45 providers and 21 pregnant women. Most of the providers were white (93%) and female (93%). A majority worked as RNs (71%); the sample included perinatal and neonatal nursery nurses, midwives, and physicians. The pregnant women were exclusively white (reflecting the rural demographic); the average age was 24 years. All the pregnant women had smoked at the beginning of their pregnancies. Four common themes emerged in both the provider and the pregnant women groups: barriers to quitting, mixed messages, approaches and attitudes, and program modalities. These themes corroborate previous findings that cigarette smoking is used for stress relief, especially when pregnancy itself is a stressor, and that pregnant women may feel guilty but don't want to be nagged or preached to. **CONCLUSION**These results have implications for how smoking cessation programs for pregnant women should be designed. Health care providers need to be cognizant of their approaches and attitudes when addressing the subject of smoking cessation. Specific educational suggestions include "putting a face" to the issue of tobacco use during pregnancy. More research is needed on how best to implement the 2008 clinical practice guideline in specific populations.

**Database:** Medline

### **13. Immune development in HIV-exposed uninfected children born to HIV-infected women.**

**Author(s):** Miyamoto, Maristela; Gouvêa, Aída F T B; Ono, Erika; Succi, Regina Célia M; Pahwa, Savita; Moraes-Pinto, Maria Isabel de

**Source:** Revista do Instituto de Medicina Tropical de Sao Paulo; Jun 2017; vol. 59 ; p. e30

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28591258

Available in full text at [Revista do Instituto de Medicina Tropical de Sao Paulo \[Rev Inst Med Trop Sao Paulo\]](#) NLMUID: 7507484 - from EBSCOhost

Available in full text at [Revista do Instituto de Medicina Tropical de São Paulo](#) - from ProQuest

**Abstract:** Immunological and clinical findings suggestive of some immune dysfunction have been reported among HIV-exposed uninfected (HEU) children and adolescents. Whether these defects are persistent or transitory is still unknown. HEU pediatric population at birth, 12 months, 6-12 years were evaluated in comparison to healthy age-matched HIV-unexposed controls. Plasma levels of LPS, sCD14, cytokines, lymphocyte immunophenotyping and T-cell receptor excision circles (TREC) were assessed. HEU and controls had similar LPS levels, which remained low from birth to 6-12 years; for plasma sCD14, IL-2, IL-6, IL-7, IL-10, IL-12p70, IL-13, IL-17, IFN- $\gamma$ , TNF- $\alpha$ , G-CSF, GM-CSF and MCP-1, which increased from birth to 12 months and then decreased at 6-12 years; and for TREC/106 PBMC at birth in HEU and controls. By contrast, plasma MIP-1 $\beta$  levels were lower in HEU than in controls ( $p=0.009$ ) at 12 months, and IL-4 levels were higher in HEU than controls ( $p=0.04$ ) at 6-12 years. Immune activation was higher in HEU at 12 months and at 6-12 years than controls based on frequencies of CD38+HLA-DR+CD8+T cells ( $p=0.05$ ) and of CD38+HLA-DR+CD4+T cells ( $p=0.006$ ). Resting memory and activated mature B cells increased from birth to 6-12 years in both groups. The development of the immune system in vertically HEU individuals is comparable to the general population in most parameters, but subtle or transient differences exist. Their role in influencing clinical incidences in HEU is unknown.

**Database:** Medline

#### **14. Hepatitis B During Pregnancy in Endemic Areas: Screening, Treatment, and Prevention of Mother-to-Child Transmission.**

**Author(s):** Chamroonkul, Naichaya; Piratvisuth, Teerha

**Source:** Paediatric drugs; Jun 2017; vol. 19 (no. 3); p. 173-181

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article Review

**PubMedID:** 28434087

**Abstract:** The proper management of pregnant women infected with hepatitis B virus (HBV) is necessary to prevent maternal and fetal morbidity and mortality and to protect the baby from HBV infection. In the majority of cases, vertical transmission can be prevented with a universal screening program, HBV vaccine immunoprophylaxis, and administration of hepatitis B immunoglobulin (HBIG) for babies born to mothers with HBV. However, in mothers with a high viral load ( $>200,000$  or  $>1,000,000$  IU/ml, depending on the guideline), the chance of immunoprophylaxis failure remains high. The standard recommendation is to give an antiviral agent during the third trimester in these patients. US FDA pregnancy category B agents such as tenofovir and telbivudine are allowed through all trimesters of pregnancy. Breastfeeding for patients who receive antiviral agents can be allowed after a risk-benefit discussion with the patient.

**Database:** Medline

#### **15. Prolactin, a potential mediator of reduced social interactive behavior in newborn infants following maternal perinatal depressive symptoms.**

**Author(s):** Zhang, Huiping; Su, Qian; Yao, Dan; Wang, Shan; Dang, Shaokang; Ding, Ding; Zhu, Zhongliang; Shao, Shuya; Li, Hui

**Source:** Journal of affective disorders; Jun 2017; vol. 215 ; p. 274-280

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28359983

**Abstract:**BACKGROUNDThe hormone prolactin (PRL) plays a crucial role for the initiation and maintenance of maternal behavior, and is also associated with the etiology of mood disorders in women, especially for depression. The present study aimed to determine whether maternal peripheral prolactin would be associated with newborn behavior disorders following maternal perinatal depressive symptoms, and further to explore the efficacy of the Newborn Behavioral Observations (NBO) in improving newborn social interactive behavior.METHODSInterview and the 24-item Hamilton Rating Scale for Depression (HAM-D) were used to assess the hospitalized pregnant women waiting for delivery at 37-42weeks of gestation. A total of 255 subjects were recruited, diagnosed with depression (n=135), and control group (n=120). Within 2 weeks postpartum, mothers were asked to fill with Maternal Attachment Inventory (MAI) to measure maternal care. Neonatal Behavioral Assessment Scale (NBAS) were used to evaluate newborn behavior. The depressed mother-newborns dyad was randomly assigned to NBO intervention and control group. Serum prolactin in mothers and cortisol in mothers and newborns were measured.RESULTSThe newborns of mothers exposed to maternal perinatal depressive symptoms displayed the reduced newborn social interactive behavior accompanied by decreased maternal serum PRL as well as increased maternal and neonatal serum cortisol. The NBO could be an effective intervention tool.LIMITATIONSOur study could not be double-blind. The mothers knew which group their infant were in.CONCLUSIONSMaternal peripheral PRL had the potential to be a mediator in reduced social interactive behavior in newborn infants following maternal perinatal depressive symptoms.

**Database:** Medline

## 16. What do dads want? Treatment preferences for paternal postpartum depression.

**Author(s):** Cameron, Emily E; Hunter, Dana; Sedov, Ivan D; Tomfohr-Madsen, Lianne M

**Source:** Journal of affective disorders; Jun 2017; vol. 215 ; p. 62-70

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28319693

**Abstract:**BACKGROUNDPostpartum depression (PPD) is prevalent, occurring in 8 to 13% of new fathers. Identifying effective and acceptable treatments for paternal PPD is important to prevent negative family outcomes. Participation in a patient preferred treatment for depression increases treatment adherence and effectiveness. Thus, developing and delivering interventions that are preferred by the target population is an important aspect of successful treatment. The current study investigated treatment preferences for paternal PPD.METHODSMen (N=140) who were within the first year postpartum were recruited from low-risk maternity clinics, baby shows, and partner referrals. Participants completed a 20-minute online survey that included three expert validated treatment descriptions for depression and a series of questionnaires.RESULTSParticipants reported preferring individual and couple psychotherapy to pharmacotherapy for treatment of PPD. Men perceived both individual and couple psychotherapy as being more credible and reported more favourable personal reactions towards them when compared to pharmacotherapy.LIMITATIONSParticipants were not required to meet diagnostic criteria for depression. The majority of participants were asked to respond to a hypothetical scenario of what

they would do if faced with PPD. **CONCLUSION** These findings suggest that fathers prefer psychological interventions over pharmacotherapy for treatment of PPD. Future research should investigate efficacious treatment options for paternal PPD based on treatment preferences.

**Database:** Medline

### **17. Development and properties of a brief scale to assess intimate partner relationship in the postnatal period.**

**Author(s):** Wynter, Karen; Tran, Thach Duc; Rowe, Heather; Fisher, Jane

**Source:** Journal of affective disorders; Jun 2017; vol. 215 ; p. 56-61

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28319692

**Abstract:** **BACKGROUND** Poor quality intimate partner relationship is associated with postnatal depression and anxiety among women. Existing scales assessing the quality of this relationship are long and measure stable aspects of the relationship rather than specific behaviours which may respond to targeted interventions. The aim was to develop and investigate the properties of a brief, life stage-specific scale to assess potentially modifiable partner behaviours in the postpartum period. **METHODS** Participants were primiparous women from diverse geographical and socio-economic backgrounds in Victoria, Australia. Seven study-specific items were developed to assess potentially modifiable aspects of the intimate partner relationship at 6 months postpartum. Women's mental health was assessed using the Composite International Diagnostic Interview and the Patient Health Questionnaire depression and generalised anxiety modules. Factor analysis was conducted on the 7 items, and associations calculated between factor scores. Factor scores were compared for women with and without mental health problems. Mean inter-item correlations were computed to assess internal consistency. **RESULTS** Factor analysis on data from 355 women revealed two factors with good internal consistency: Caring Partner Behaviours and Emotionally Abusive Partner Behaviours. Having mental health problems was associated with lower Caring Partner Behaviours and higher Emotionally Abusive Partner Behaviours scores. **LIMITATIONS** Interaction between partners was not observed; thus external criterion validity was not assessed. **CONCLUSION** This brief scale is a promising means of assessing potentially modifiable aspects of the intimate partner relationship in the postnatal period.

**Database:** Medline

### **18. Trajectories of maternal depressive symptoms in the early childhood period and family-wide clustering of risk.**

**Author(s):** Madigan, Sheri; Wade, Mark; Plamondon, André; Jenkins, Jennifer M

**Source:** Journal of affective disorders; Jun 2017; vol. 215 ; p. 49-55

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28319691

**Abstract:** **BACKGROUND** Previous research on individual differences in the course of maternal depressive symptoms has yielded inconsistent findings, with significant variation in the number and pattern of trajectories identified. In addition, missing from the literature is a comprehensive examination of predictors and longitudinal consequences of particular depression trajectories. **METHOD** Participants in this study included a community cohort of 501 women assessed

for depression using the Center for Epidemiologic Depression Scale at infant age 2, 18, 36, and 54 months. A multi-informant approach was used to examine predictors and outcomes of trajectory membership. RESULTS Using growth mixture modeling, three distinct trajectories emerged: 84% of the sample demonstrated low-stable levels of depressive symptoms, 9.5% had high-decreasing scores, and 6.5% had moderate-increasing scores. While socioeconomic status and marital conflict differentiated the low-stable group from the high-decreasing and moderate-increasing group, neighborhood collective efficacy differentiated the latter two groups. At 54 months, a clustering of family risks was prevalent for the moderate-increasing depression group, including higher marital conflict and household chaos, lower parental positivity, and heightened levels of child psychopathology. LIMITATIONS Limitations include reliance on self-reports to assess maternal depression and the relatively small sample size of certain trajectory classes. CONCLUSIONS The onset and course of maternal depression in the early childrearing period is heterogeneous, with distinct subgroups in the population. Comprehensive assessment of individual, family, and neighborhood stressors augments our understanding of the predictors and consequences of trajectory membership over this critical period of child and family adaptation.

**Database:** Medline

### **19. Association Between Maternal Smoking During Pregnancy and Severe Mental Illness in Offspring.**

**Author(s):** Quinn, Patrick D; Rickert, Martin E; Weibull, Caroline E; Johansson, Anna L V; Lichtenstein, Paul; Almqvist, Catarina; Larsson, Henrik; Iliadou, Anastasia N; D'Onofrio, Brian M

**Source:** JAMA psychiatry; Jun 2017; vol. 74 (no. 6); p. 589-596

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28467540

Available in full text at [JAMA psychiatry \[JAMA Psychiatry\] NLMUID: 101589550](#) - from EBSCOhost

**Abstract:** Importance Several recent population-based studies have linked exposure to maternal smoking during pregnancy to increased risk of severe mental illness in offspring (eg, bipolar disorder, schizophrenia). It is not yet clear, however, whether this association results from causal teratogenic effects or from confounding influences shared by smoking and severe mental illness. Objective To examine the association between smoking during pregnancy and severe mental illness in offspring, adjusting for measured covariates and unmeasured confounding using family-based designs. Design, Setting, and Participants This study analyzed population register data through December 31, 2013, for a cohort of 1 680 219 individuals born in Sweden from January 1, 1983, to December 31, 2001. Associations between smoking during pregnancy and severe mental illness in offspring were estimated with adjustment for measured covariates. Cousins and siblings who were discordant on smoking during pregnancy and severe mental illness were then compared, which helped to account for unmeasured genetic and environmental confounding by design. Exposures Maternal self-reported smoking during pregnancy, obtained from antenatal visits. Main Outcomes and Measures Severe mental illness, with clinical diagnosis obtained from inpatient and outpatient visits and defined using International Classification of Diseases codes for bipolar disorder and schizophrenia spectrum disorders. Results Of the 1 680 219 offspring included in the analysis, 816 775 (48.61%) were female. At the population level, offspring exposed to moderate and high levels of smoking during pregnancy had greater severe mental illness rates than did unexposed offspring (moderate smoking during pregnancy: hazard ratio [HR], 1.25; 95% CI, 1.19-1.30; high smoking during pregnancy: HR, 1.51; 95% CI, 1.44-1.59). These associations decreased in strength with increasing statistical and methodologic controls for familial confounding. In sibling comparisons with within-family covariates, associations were substantially weaker and nonsignificant (moderate smoking during pregnancy: HR, 1.09; 95%

CI, 0.94-1.26; high smoking during pregnancy: HR, 1.14; 95% CI, 0.96-1.35). The pattern of associations was consistent across subsets of severe mental illness disorders and was supported by further sensitivity analyses. **Conclusions and Relevance** This population- and family-based study failed to find support for a causal effect of smoking during pregnancy on risk of severe mental illness in offspring. Rather, these results suggest that much of the observed population-level association can be explained by measured and unmeasured factors shared by siblings.

**Database:** Medline

## **20. Screening for early-onset invasive group B Streptococcal disease in neonates in an Irish hospital (2001-2014): a retrospective audit.**

**Author(s):** Nielsen, Maryke; Sheikh, Naveed; Fitzgerald, Eoin; Meehan, Mary; LeBlanc, David; Eogan, Maeve; El-Khuffash, Afif; Drew, Richard J

**Source:** Infectious diseases (London, England); Jun 2017; vol. 49 (no. 6); p. 466-470

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28276804

**Abstract:** Group B Streptococcus (GBS) is the most common cause of early-onset neonatal sepsis and meningitis. In babies with no clinical suspicion of infection, who are at risk of early-onset invasive disease based on maternal risk factors, blood cultures are taken to detect bacteraemia. In our institution, lumbar punctures are performed in infants with clinical signs of sepsis but not in infants who are well at the time of screening. Between 2001 and 2014, there were 112,361 live births weighing >500 g, of whom 13,959 (12.4%) infants had a blood culture taken on the first or second day of life, and 1971 (14.1%) of these infants had lumbar punctures on these first two days of life. Fifty-three cases of early-onset GBS disease were identified. Only three patients with invasive GBS disease had no clinical suspicion for sepsis at the time of testing. Thus, the number of blood cultures taken to detect one case of GBS bacteraemia in an infant who is well at the time of testing was 3996.

**Database:** Medline

## **21. The use of biologics in pregnant patients with rheumatic disease.**

**Author(s):** Østensen, Monika

**Source:** Expert review of clinical pharmacology; Jun 2017; vol. 10 (no. 6); p. 661-669

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article Review

**PubMedID:** 28326845

**Abstract:** **INTRODUCTION** An increasing number of female patients with autoimmune diseases are treated with biologic drugs. Concerns in regard to safety of biologics during pregnancy arise in patients who have not completed their families. **Areas covered:** A review of the literature dealing with child outcomes of pregnancies exposed to biologics shows that TNF inhibitors (TNFi) are the best studied in regard to human pregnancy. In studies comparing exposed pregnancies to disease-matched controls no increased risk of spontaneous abortion, low birth weight, prematurity or congenital malformations has been observed. For rituximab, tocilizumab, anakinra, belimumab and ustekinumab no prospective, controlled studies are available, and firm conclusions about their safety during pregnancy cannot be drawn. **Expert commentary:** TNFi appear fairly safe when given in early pregnancy. For biologics other than TNFi prospective, controlled studies on outcomes after early and late pregnancy exposure are urgently needed. Possible effects of TNFi and all other biologics on

children's immune function, infection rate and vaccination responses are either limited or absent and need to be extended. Development of laboratory tests to measure concentrations of biologics routinely in children exposed in utero would facilitate decisions in regard to the time point of vaccination with live vaccines.

**Database:** Medline

## 22. Medical problems in pregnancy.

**Author(s):** Narayan, Bhaskar; Nelson-Piercy, Catherine

**Source:** Clinical medicine (London, England); Jun 2017; vol. 17 (no. 3); p. 251-257

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article Review

**PubMedID:** 28572227

Available in full text at [Clinical medicine: journal of the Royal College of Physicians of London \[Clin Med \(Lond\)\] NLMUID: 101092853](#) - from EBSCOhost

Available in full text at [Clinical Medicine](#) - from ProQuest

**Abstract:**The prevalence of medical problems in pregnancy is increasing because of a complex interplay between demographic and lifestyle factors, and developments in modern medicine. Maternal mortality and morbidity resulting from treatable medical conditions, such as venous thromboembolism, epilepsy and autoimmune disease, have not decreased in recent years. This is despite a marked decrease in overall maternal mortality. It is vital that all physicians acquire a basic knowledge and understanding of medical problems in pregnancy. This includes prepregnancy measures such as counselling and optimisation of medical therapy, as well as multidisciplinary management throughout pregnancy and the postpartum period. Prompt recognition and treatment of acute and chronic illness is of clear benefit, and most drugs and many radiological investigations may be used in pregnancy.

**Database:** Medline

## 23. Maternal fetal loss history and increased acute leukemia subtype risk in subsequent offspring: a systematic review and meta-analysis.

**Author(s):** Karalexi, M A; Dessypris, N; Skalkidou, A; Biniaris-Georgallis, S -I; Kalogirou, E I; Thomopoulos, T P; Herlenius, E; Spector, L G; Loutradis, D; Chrousos, G P; Petridou, E Th

**Source:** Cancer causes & control : CCC; Jun 2017; vol. 28 (no. 6); p. 599-624

**Publication Date:** Jun 2017

**Publication Type(s):** Meta-analysis Journal Article Review

**PubMedID:** 28401353

**Abstract:**PURPOSEHistory of fetal loss including miscarriage and stillbirth has been inconsistently associated with childhood (0-14 years) leukemia in subsequent offspring. A quantitative synthesis of the inconclusive literature by leukemia subtype was therefore conducted.METHODSEligible studies (N = 32) were identified through the screening of over 3500 publications. Random-effects meta-analyses were conducted on the association of miscarriage/stillbirth history with overall (AL; 18,868 cases/35,685 controls), acute lymphoblastic (ALL; 16,150 cases/38,655 controls), and myeloid (AML; 3042 cases/32,997 controls) leukemia. Sensitivity and subgroup analyses by age and ALL subtype, as well as meta-regression were undertaken.RESULTSFetal loss history was associated with increased AL risk [Odds Ratio (OR) 1.10, 95% Confidence Intervals (CI) 1.04-1.18]. The positive association was



seen for ALL (OR 1.12, 95%CI 1.05-1.19) and for AML (OR 1.13, 95%CI 0.91-1.41); for the latter the OR increased in sensitivity analyses. Notably, stillbirth history was significantly linked to ALL risk (OR 1.33, 95%CI 1.02-1.74), but not AML. By contrast, the association of ALL and AML with previous miscarriage reached marginal significance. The association of miscarriage history was strongest in infant ALL (OR 2.34, 95%CI 1.19-4.60). **CONCLUSIONS**In this meta-analysis involving >50,000 children, we found noteworthy associations by indices of fetal loss, age at diagnosis, and leukemia type; namely, of stillbirth with ALL and miscarriage history with infant ALL. Elucidation of plausible underlying mechanisms may provide insight into leukemia pathogenesis and indicate monitoring interventions prior to and during pregnancy.

**Database:** Medline

#### **24. Anemia and Dental Caries in Pregnant Women: a Prospective Cohort Study.**

**Author(s):** Costa, Elisa Miranda; Azevedo, Juliana A P; Martins, Rafiza F M; Alves, Cláudia M C; Ribeiro, Cecília C C; Thomaz, Erika B A F

**Source:** Biological trace element research; Jun 2017; vol. 177 (no. 2); p. 241-250

**Publication Date:** Jun 2017

**Publication Type(s):** Journal Article

**PubMedID:** 27866358

**Abstract:**The objective was to evaluate the effect of anemia during pregnancy on the risk of dental caries development in pregnant women. A prospective cohort including a sample of pregnant women in a prenatal care unit of São Luís, Brazil, was done. The incidence of dental caries during pregnancy, according to Nyvad's criteria, was the outcome. The main independent variables were serum iron, ferritin, hemoglobin, erythrocyte, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW). Pregnant women (n = 121) were evaluated at two moments: up to 16th week of gestational age (T1) and in the last trimester of pregnancy (T2). Crude and adjusted associations were estimated by the incidence ratio risk (IRR) and respective 95% confidence intervals (95%CI). After adjustment, higher serum concentrations of ferritin (IRR = 0.97, 95%CI 0.95-0.99) in T1, and Fe (IRR = 0.99, 95%CI 0.98-0.99), ferritin (IRR = 0.99, 95%CI 0.98-0.99), erythrocyte (IRR = 0.71, 95%CI 0.50-0.99), hemoglobin (IRR = 0.84, 95%CI 0.73-0.96), hematocrit (IRR = 0.93, 95%CI 0.88-0.98), MCV (IRR = 0.91, 95%CI 0.86-0.96), and MCH (IRR = 0.83, 95%CI 0.74-0.93) in T2, were associated with fewer incidence of dental caries in pregnant women. Iron deficiency anemia during pregnancy is a risk factor for the incidence of dental caries in these women.

**Database:** Medline

#### **25. Prenatal antidepressant use and risk of attention-deficit/hyperactivity disorder in offspring: population based cohort study.**

**Author(s):** Man, Kenneth K C; Chan, Esther W; Ip, Patrick; Coghill, David; Simonoff, Emily; Chan, Phyllis K L; Lau, Wallis C Y; Schuemie, Martijn J; Sturkenboom, Miriam C J M; Wong, Ian C K

**Source:** BMJ (Clinical research ed.); May 2017; vol. 357 ; p. j2350

**Publication Date:** May 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28566274

Available in full text at [The BMJ](#) - from Highwire Press

**Abstract:** Objective To assess the potential association between prenatal use of antidepressants and the risk of attention-deficit/hyperactivity disorder (ADHD) in offspring. Design Population based cohort study. Setting Data from the Hong Kong population based electronic medical records on the Clinical Data Analysis and Reporting System. Participants 190 618 children born in Hong Kong public hospitals between January 2001 and December 2009 and followed-up to December 2015. Main outcome measure Hazard ratio of maternal antidepressant use during pregnancy and ADHD in children aged 6 to 14 years, with an average follow-up time of 9.3 years (range 7.4-11.0 years). Results Among 190 618 children, 1252 had a mother who used prenatal antidepressants. 5659 children (3.0%) were given a diagnosis of ADHD or received treatment for ADHD. The crude hazard ratio of maternal antidepressant use during pregnancy was 2.26 ( $P < 0.01$ ) compared with non-use. After adjustment for potential confounding factors, including maternal psychiatric disorders and use of other psychiatric drugs, the adjusted hazard ratio was reduced to 1.39 (95% confidence interval 1.07 to 1.82,  $P = 0.01$ ). Likewise, similar results were observed when comparing children of mothers who had used antidepressants before pregnancy with those who were never users (1.76, 1.36 to 2.30,  $P < 0.01$ ). The risk of ADHD in the children of mothers with psychiatric disorders was higher compared with the children of mothers without psychiatric disorders even if the mothers had never used antidepressants (1.84, 1.54 to 2.18,  $P < 0.01$ ). All sensitivity analyses yielded similar results. Sibling matched analysis identified no significant difference in risk of ADHD in siblings exposed to antidepressants during gestation and those not exposed during gestation (0.54, 0.17 to 1.74,  $P = 0.30$ ). Conclusions The findings suggest that the association between prenatal use of antidepressants and risk of ADHD in offspring can be partially explained by confounding by indication of antidepressants. If there is a causal association, the size of the effect is probably smaller than that reported previously.

**Database:** Medline

## 26. Pregabalin use early in pregnancy and the risk of major congenital malformations.

**Author(s):** Paterno, Elisabetta; Bateman, Brian T; Huybrechts, Krista F; MacDonald, Sarah C; Cohen, Jacqueline M; Desai, Rishi J; Panchaud, Alice; Mogun, Helen; Pennell, Page B; Hernandez-Diaz, Sonia

**Source:** Neurology; May 2017; vol. 88 (no. 21); p. 2020-2025

**Publication Date:** May 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28446648

Available in full text at [Neurology](#) - from Ovid

**Abstract:** OBJECTIVE To assess whether first-trimester exposure to pregabalin is associated with an increased risk of major congenital malformations, as recently suggested in a pregnancy registry study. METHODS We performed a cohort study nested in the US Medicaid Analytic eXtract (MAX). The study population included 1,323,432 pregnancies resulting in a live-born infant between 2000 and 2010. We examined the risk of major congenital malformations among infants born to women exposed to pregabalin during the first trimester compared with women unexposed to anticonvulsants. We used propensity score fine stratification to control for >50 potential confounders, and we estimated relative risks (RRs) and 95% confidence intervals (CIs) in generalized linear models. The analyses were replicated in the Truven Health MarketScan Commercial Database (MarketScan). Pooled estimates based on the adjusted RR produced in MAX, MarketScan, and the previous registry study were calculated. RESULTS Of 477 infants exposed to pregabalin during the first trimester in MAX, 28 (5.9%) had malformations compared to 3.3% in nonexposed infants. The crude RR of major congenital malformations for pregabalin was 1.80 (95% CI 1.26-2.58). After propensity score adjustment, the RR moved to 1.16 (95% CI 0.81-1.67). Restriction to pregabalin monotherapy and sensitivity analyses produced similar results. The adjusted RR for major congenital

malformations for the 174 infants exposed in MarketScan was 1.03 (95% CI 0.56-1.90). The pooled RR was 1.33 (95% CI 0.83-2.15) for pregabalin any use and 1.02 (95% CI 0.69-1.51) for pregabalin monotherapy. CONCLUSIONS Findings did not confirm the suggested teratogenic effects of pregabalin, although they cannot rule out the possibility of a small effect.

**Database:** Medline

### **27. Impairment of microvascular angiogenesis is associated with delay in prostatic development in rat offspring of maternal protein malnutrition.**

**Author(s):** Colombelli, Ketlin T; Santos, Sérgio A A; Camargo, Ana C L; Constantino, Flávia B; Barquilha, Caroline N; Rinaldi, Jaqueline C; Felisbino, Sérgio L; Justulin, Luis A

**Source:** General and comparative endocrinology; May 2017; vol. 246 ; p. 258-269

**Publication Date:** May 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28041790

**Abstract:** Experimental data demonstrated the negative impact of maternal protein malnutrition (MPM) on rat prostate development, but the mechanism behind the impairment of prostate growth has not been well understood. Male Sprague Dawley rats, born to dams fed a normal protein diet (CTR group, 17% protein diet), were compared with those born to dams fed a low protein diet (6% protein diet) during gestation (GLP group) or gestation and lactation (GLLP). The ventral prostate lobes (VP) were removed at post-natal day (PND) 10 and 21, and analyzed via different methods. The main findings were low birth weight, a reduction in ano-genital distance (AGD, a testosterone-dependent parameter), and an impairment of prostate development. A delay in prostate morphogenesis was associated with a reduced testosterone levels and angiogenic process through downregulation of aquaporin-1 (AQP-1), insulin/IGF-1 axis and VEGF signaling pathway. Depletion of the microvascular network, which occurs in parallel to the impairment of proliferation and differentiation of the epithelial cells, affects the bidirectional flux between blood vessels impacting prostatic development. In conclusion, our data support the hypothesis that a reduction in microvascular angiogenesis, especially in the subepithelial compartment, is associated to the impairment of prostate morphogenesis in the offspring of MPM dams.

**Database:** Medline

### **28. Perinatal outcomes in multifetal pregnancy following fetal reduction.**

**Author(s):** Razaz, Neda; Avitan, Tehila; Ting, Joseph; Pressey, Tracy; Joseph, K S

**Source:** CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne; May 2017; vol. 189 (no. 18); p. E652

**Publication Date:** May 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28483844

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Available in full text at [CMAJ: Canadian Medical Association journal = journal de l'Association medicale canadienne \[CMAJ\]](#) NLMUID: 9711805 - from EBSCOhost

**Abstract:**BACKGROUND There is currently insufficient evidence regarding the prognosis of multifetal pregnancy following elective fetal reduction to twin or singleton pregnancy. We compared perinatal outcomes in pregnancies with and without fetal reduction. METHODS We used data on all stillbirths and live births in British Columbia, Canada, from 2009 to 2013. We compared outcomes of multifetal pregnancies with fetal reduction (to twin or singleton pregnancy) with outcomes of pregnancies without fetal reduction. The primary outcome was a composite of serious neonatal morbidity or perinatal death. Other outcomes studied included preterm birth, low birth weight and small-for-gestational-age live birth. RESULT The rate of serious neonatal morbidity or perinatal death did not differ significantly between pregnancies reduced to twins and unreduced triplet pregnancies (adjusted rate ratio 0.50, 95% confidence interval [CI] 0.24-1.07) or between pregnancies reduced to singletons and unreduced twin pregnancies (adjusted rate ratio 1.57, 95% CI 0.74-3.33). The rate was significantly lower in the fetal reduction group reduced to twins versus unreduced triplet pregnancies when we restricted the analysis to pregnancies conceived following the use of assisted reproduction technologies (adjusted rate ratio 0.35, 95% CI 0.18-0.67). The rates of preterm birth, very preterm birth, low birth weight and very low birth weight were significantly lower among pregnancies reduced to twins than among unreduced triplet pregnancies. Compared with unreduced twin pregnancies, pregnancies reduced to singletons had lower rates of preterm birth and low birth weight. INTERPRETATION Fetal reduction to twins and singletons was not associated with a decreased risk of serious neonatal morbidity or perinatal death. However, such fetal reduction was associated with substantial improvements in several other perinatal outcomes, such as preterm birth and low birth weight. Clinicians discussing the risks associated with multifetal pregnancy should counsel parents on the potential risks and benefits of fetal reduction.

**Database:** Medline

## 29. Clinical and Microbiologic Characteristics of Early-onset Sepsis Among Very Low Birth Weight Infants: Opportunities for Antibiotic Stewardship.

**Author(s):** Mukhopadhyay, Sagori; Puopolo, Karen M

**Source:** The Pediatric infectious disease journal; May 2017; vol. 36 (no. 5); p. 477-481

**Publication Date:** May 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28403049

**Abstract:**BACKGROUND Most very low birth weight (VLBW, birth weight <1500 g) infants receive empiric antibiotics for risk of early-onset sepsis (EOS). The objective of this study was to determine the characteristics of VLBW infants with culture-confirmed EOS at a single center during 25 years and to identify opportunities for antibiotic stewardship. METHODS Retrospective cohort study includes VLBW infants admitted from 1990 to 2015. EOS was defined as isolation of a pathogen in blood or cerebrospinal fluid culture obtained at <72 hours of age. Clinical and microbiologic characteristics of EOS case infants were obtained by review of medical, laboratory and administrative records. Blood culture, antibiotic initiation and maternal discharge code data were available for all VLBW infants born between 1999 and 2013. RESULT One-hundred nine EOS cases (20.5/1000 VLBW births) occurred during the study period. Preterm labor, preterm rupture of membranes and/or the obstetrical diagnosis of chorioamnionitis were present in 106/109 cases (97%). Obligate anaerobic organisms accounted for 16% of cases. Time to culture positivity was 36 hours for 88% and 48 hours for 98% of cases. From 1999 to 2013, 97% of VLBW infants were evaluated for EOS and 90% administered empiric antibiotics; 22% of these infants were born by cesarean section to mothers with preeclampsia and without preterm labor or chorioamnionitis and had a 12-fold lower incidence of EOS compared with the remaining infants. CONCLUSION Decisions to

initiate and discontinue empiric antibiotics among VLBW infants can be informed by the delivery characteristics of infected infants and by local microbiologic data.

**Database:** Medline

### **30. New Predictive Model at 11+0 to 13+6 Gestational Weeks for Early-Onset Preeclampsia With Fetal Growth Restriction.**

**Author(s):** Chang, Ying; Chen, Xu; Cui, Hong-Yan; Li, Xing; Xu, Ya-Ling

**Source:** Reproductive sciences (Thousand Oaks, Calif.); May 2017; vol. 24 (no. 5); p. 783-789

**Publication Date:** May 2017

**Publication Type(s):** Journal Article

**PubMedID:** 27678097

**Abstract:**The aim of the present study was to determine a predictive model for early-onset preeclampsia with fetal growth restriction (FGR) to be used at 11+0 to 13+6 gestational weeks, by combining the maternal serum level of pregnancy-associated plasma protein-A (PAPP-A), placental growth factor (PLGF), placental protein 13 (PP13), soluble endoglin (sEng), mean arterial pressure (MAP), and uterine artery Doppler. This was a retrospective cohort study of 4453 pregnant women. Uterine artery Doppler examination was conducted in the first trimester. Maternal serum PAPP-A, PLGF, PP13, and sEng were measured. Mean arterial pressure was obtained. Women were classified as with/without early-onset preeclampsia, and women with preeclampsia were classified as with/without FGR. Receiver operating characteristic analysis was performed to determine the value of the model. There were 30 and 32 pregnant women with early-onset preeclampsia with and without FGR. The diagnosis rate of early-onset preeclampsia with FGR was 67.4% using the predictive model when the false positive rate was set at 5% and 73.2% when the false positive rate was 10%. The predictive model (MAP, uterine artery Doppler measurements, and serum biomarkers) had some predictive value for the early diagnosis (11+0 to 13+6 gestational weeks) of early-onset preeclampsia with FGR.

**Database:** Medline



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