TY - GEN
AB - The ophthalmic artery is an easily accessible vessel for Doppler assessment that provides information on the less accessible intracranial circulation. In women with preeclampsia, compared with normotensive pregnant women, there is a decrease in impedance to flow and an increase in velocities in the flow velocity waveforms from the ophthalmic arteries. This study aimed to report the methodology for ophthalmic artery Doppler and summarize findings from the clinical implementation of such assessment in the prediction of preeclampsia. The Embase and MEDLINE were searched from inception to November 2020 to identify studies reporting on the use of ophthalmic artery Doppler in the prediction of preeclampsia. Of note, 2 small studies in high-risk pregnancies, one at 11 to 14 weeks' gestation and another at 20 to 28 weeks' gestation, reported differences between women who developed preeclampsia, compared with unaffected pregnancies, in ophthalmic artery Doppler and suggested that this is a useful biomarker for screening for preeclampsia. Another small study in high-risk pregnancies at 18 to 23 weeks' gestation reported that there was no marked difference in ophthalmic artery Doppler indices between the preeclampsia and unaffected groups. In addition, 2 recent, large observational studies in unselected pregnancies at 19 to 23 and 35 to 37 weeks' gestation, respectively, reported that, first, it is necessary to record waveforms from both eyes to get reproducible results; second, the waveform from the ophthalmic arteries is characterized by 2 systolic peaks and the ratio of the second to the first peak systolic velocity was increased in women who developed preeclampsia; third, in the study at 19 to 23 weeks' gestation, the peak systolic velocity ratio was superior to the uterine artery pulsatility index, mean arterial pressure, serum placental growth factor, and soluble fms-like tyrosine kinase-1 as individual biomarkers in the prediction of both preterm and term preeclampsia and the peak systolic velocity ratio improved the prediction of preeclampsia provided by all the other biomarkers; and fourth, in the study at 35 to 37 weeks' gestation, the peak systolic velocity ratio improved the prediction of subsequent development of preeclampsia provided by maternal factors alone and combinations of maternal factors with mean arterial pressure, uterine artery pulsatility index, placental growth factor, and serum placental growth factor. The ophthalmic artery Doppler provides a useful biomarker for the prediction of preeclampsia.
AU - Nicolaides, Kypros H.
AU - Sarno, Manoel
AU - Wright, Alan
DA - 2022/2//
DO - 10.1016/j.ajog.2020.11.039
IS - 2
KW - biomarker
KW - competing risks model
KW - mean arterial pressure
KW - peak systolic velocity
KW - placental growth factor
KW - sensitivity
KW - soluble fms-like tyrosine kinase-1
KW - uterine artery
PB - Elsevier Inc.
PY - 2022
SP - S1098

EP - S1101
TI - Ophthalmic artery Doppler in the prediction of preeclampsia
T2 - American Journal of Obstetrics and Gynecology
VL - 226
ER -
TY - GEN
AB - Objective: To determine the accuracy of ophthalmic artery Doppler in pregnancy for the prediction of pre-eclampsia (PE). Methods: MEDLINE, EMBASE, CINAHL and The Cochrane Library were searched for relevant citations without language restrictions. Two reviewers independently selected studies that evaluated the accuracy of ophthalmic artery Doppler to predict the development of PE and extracted data to construct 2 × 2 tables. Individual patient data were obtained from the authors if available. A bivariate random-effects model was used for the quantitative synthesis of data. Logistic regression analysis was employed to generate receiver–operating characteristics (ROC) curves and obtain optimal cut-offs for each investigated parameter, and a bivariate analysis was employed using predetermined cut-offs to obtain sensitivity and specificity values and generate summary ROC curves. Results: A total of 87 citations matched the search criteria of which three studies, involving 1119 pregnancies, were included in the analysis. All included studies had clear description of the index and reference tests, avoidance of verification bias and adequate follow-up. Individual patient data were obtained for all three included studies. First diastolic peak velocity of ophthalmic artery Doppler at a cut-off of 23.3 cm/s showed modest sensitivity (61.0%; 95% CI, 44.2–76.1%) and specificity (73.2%; 95% CI, 66.9–78.7%) for the prediction of early-onset PE (area under the ROC curve (AUC), 0.68; 95% CI, 0.61–0.76). The first diastolic peak velocity had a much lower sensitivity (39.0%; 95% CI, 20.6–61.0%), a similar specificity (73.2%; 95% CI, 66.9–78.7%) and a lower AUC (0.58; CI, 0.52–0.65) for the prediction of late-onset PE. The pulsatility index of the ophthalmic artery did not show a clinically useful sensitivity or specificity at any cut-off for early- or late-onset PE. Peak ratio above 0.65 showed a similar diagnostic accuracy to that of the first diastolic peak velocity with an AUC of 0.67 (95% CI, 0.58–0.77) for early-onset PE and 0.57 (95% CI, 0.51–0.63) for late-onset disease. Conclusions: Ophthalmic artery Doppler is a simple, accurate and objective technique with a standalone predictive value for the development of early-onset PE equivalent to that of uterine artery Doppler evaluation. The relationship between ophthalmic Doppler indices and PE cannot be a consequence of trophoblast invasion and may be related to maternal hemodynamic adaptation to pregnancy. The findings of this review justify efforts to elucidate the effectiveness and underlying mechanism whereby two seemingly unrelated maternal vessels can be used for the prediction of a disease considered a ‘placental disorder’.
AU - Kalafat, E.
AU - Laoreti, A.
AU - Khalil, A.
AU - Da Silva Costa, F.
AU - Thilaganathan, B.
DA - 2018/6//
DO - 10.1002/uog.19002
IS - 6
KW - Doppler

KW - ophthalmic artery
KW - peak ratio
KW - placentation
KW - pre-eclampsia
KW - uterine artery
PB - John Wiley and Sons Ltd
PY - 2018
SP - 731
EP - 737
TI - Ophthalmic artery Doppler for prediction of pre-eclampsia: systematic review and meta-analysis
T2 - Ultrasound in Obstetrics and Gynecology
VL - 51
ER -
TY - JOUR
AB - Objective: In mid-gestation, the finding of an increase in the ophthalmic artery second to first peak of systolic velocity ratio (PSV ratio) provides useful prediction of subsequent development of pre-eclampsia (PE). The objective of this study of an unselected population at 19–23 weeks' gestation was to gain a better understanding of the factors that influence ophthalmic artery Doppler by examining the possible association between the PSV ratio and maternal cardiovascular function. Methods: This was a prospective observational study in women attending for a routine hospital visit at 19 + 1 to 23 + 3 weeks' gestation. This visit included assessment of flow velocity waveforms from the maternal ophthalmic arteries and assessment of maternal cardiovascular function. The following nine cardiovascular indices were examined: E/A ratio; E/e’ ratio; myocardial performance index; global longitudinal systolic strain; left ventricular ejection fraction; peripheral vascular resistance; left ventricular cardiac output; left ventricular mass indexed for body surface area; and mean arterial pressure. The ophthalmic artery PSV ratio and the nine cardiovascular indices were converted to either log10 multiples of the median (MoM) values or deviations from the median (deltas) values after adjustment for maternal characteristics and elements of medical history. Regression analysis was then used to examine the significance of the association between PSV ratio delta and MoM or delta values of each cardiovascular index in the total population and in the subgroup that developed PE. Results: The study population of 2853 pregnancies contained 76 (2.7%) that developed PE. In the total population, there were significant but weak associations between the PSV ratio and most of the cardiovascular indices, with r-values of < 0.1, except for mean arterial pressure with r = 0.178. In the subgroup that developed PE, a moderately strong association between the PSV ratio and left ventricular mass indexed for body surface area was noted (r = 0.308). Conclusions: The findings of this study suggest that Doppler assessment of PSV ratio in the ophthalmic artery provides information about peripheral vascular status. The increase in PSV ratio in women who develop PE is associated with increased afterload and an increase in left ventricular thickness. © 2021 International Society of Ultrasound in Obstetrics and Gynecology.
AU - Gibbone, E.
AU - Sapantzoglou, I.
AU - Nuñez-Cerrato, M. E.
AU - Wright, A.
AU - Nicolaides, K. H.

AU - Charakida, M.
DA - 2021/5//
DO - 10.1002/uog.23601
IS - 5
KW - maternal cardiovascular function
KW - ophthalmic artery Doppler
KW - pre-eclampsia
PB - John Wiley and Sons Ltd
PY - 2021
SP - 733
EP - 738
TI - Relationship between ophthalmic artery Doppler and maternal cardiovascular function
T2 - Ultrasound in Obstetrics and Gynecology
VL - 57
ER -
TY - GEN
AU - Gonser, M.
AU - Vonzun, L.
AU - Ochsenbein-Kölble, N.
DA - 2022/3//
DO - 10.1002/uog.24845
IS - 3
PB - John Wiley and Sons Ltd
PY - 2022
SP - 402
EP - 404
TI - Association of ophthalmic artery Doppler and maternal cardiac changes in preclinical stage of pre-eclampsia: hemodynamic relationship
T2 - Ultrasound in Obstetrics and Gynecology
VL - 59
ER -
TY - GEN
AU - Gonser, M.
AU - Vonzun, L.
AU - Ochsenbein-Kölble, N.
DA - 2021/7//
DO - 10.1002/uog.23665
IS - 1
PB - NLM (Medline)
PY - 2021
SP - 145
EP - 147
TI - Ophthalmic artery Doppler in prediction of pre-eclampsia: insights from hemodynamic considerations
T2 - Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology
VL - 58
ER -
TY - JOUR

AB - Objective: To investigate dynamic changes in myometrial thickness during the third stage of labor. Methods: Myometrial thickness was measured using ultrasound at one-minute time intervals during the third stage of labor in the mid-region of the upper and lower uterine segments in 151 patients including: women with a long third stage of labor (n = 30), postpartum hemorrhage (n = 4), preterm delivery (n = 7) and clinical chorioamnionitis (n = 4). Differences between myometrial thickness of the uterine segments and as a function of time were evaluated. Results: There was a significant linear increase in the mean myometrial thickness of the upper uterine segments, as well as a significant linear decrease in the mean myometrial thickness of the lower uterine segments until the expulsion of the placenta ($p < 0.001$). The ratio of the measurements of the upper to the lower uterine segments increased significantly as a function of time ($p < 0.0001$). In women with postpartum hemorrhage, preterm delivery, and clinical chorioamnionitis, an uncoordinated pattern among the uterine segments was observed. Conclusion: A well-coordinated activity between the upper and lower uterine segments is demonstrated in normal placental delivery. In some clinical conditions this pattern is not observed, increasing the time for placental delivery and the risk of postpartum hemorrhage.
AU - Patwardhan, Manasi
AU - Hernandez-Andrade, Edgar
AU - Ahn, Hyunyoung
AU - Korzeniewski, Steven J.
AU - Schwartz, Alyse
AU - Hassan, Sonia S.
AU - Romero, Roberto
DA - 2015/7//
DO - 10.1159/000370001
IS - 1
KW - Clinical chorioamnionitis
KW - Labor
KW - Myometrial thickness
KW - Postpartum hemorrhage
KW - Pregnancy
KW - Preterm delivery
KW - Prolonged third stage of labor
KW - Uterine contractions
PB - S. Karger AG
PY - 2015
SP - 26
EP - 37
TI - Dynamic Changes in the Myometrium during the Third Stage of Labor, Evaluated Using Two-Dimensional Ultrasound, in Women with Normal and Abnormal Third Stage of Labor and in Women with Obstetric Complications
T2 - Gynecologic and Obstetric Investigation
VL - 80
ER -
TY - GEN
AB - Postpartum haemorrhage (PPH) is a potential cause of maternal mortality, and obstetricians must be prepared to rapidly diagnose and treat this condition. Optimal treatment is dependent upon the underlying cause of haemorrhage.

Ultrasonography is the most helpful tool for prompt diagnosis of PPH aetiology and obstetricians must have a strong understanding of postpartum ultrasonography. In our previous report, we demonstrated the utility of ultrasonography using the focused assessment with sonography for obstetrics (FASO) technique (a modified version of FAST) as the primary postpartum obstetric survey. In the present article, we review the ultrasonographic findings of PPH, differentiated by the underlying cause of haemorrhage, including retained placenta, morbidly adherent placenta, uterine rupture, uterine inversion and uterine artery abnormalities.
AU - Oba, Tomohiro
AU - Hasegawa, Junichi
AU - Sekizawa, Akihiko
DA - 2017/7//
DO - 10.1080/14767058.2016.1223034
IS - 14
KW - Postpartum ultrasound
KW - advanced life support
KW - differential diagnosis
KW - maternal mortality
KW - postpartum haemorrhage
PB - Taylor and Francis Ltd
PY - 2017
SP - 1726
EP - 1729
TI - Postpartum ultrasound: postpartum assessment using ultrasonography
T2 - Journal of Maternal-Fetal and Neonatal Medicine
VL - 30
ER -
TY - JOUR
AB - Objectives: To determine whether there is a relationship between the findings of routine postpartum ultrasonographic scanning and puerperal uterine complications such as heavy delayed postpartum hemorrhage, retained products of conception, and need for uterine curettage; and to estimate the value of both routine ultrasonographic scanning and clinical data in the prediction of these complications. Methods: In this cohort study 265 women were examined ultrasonographically on postpartum Days 1, 14, 42 following uncomplicated vaginal or cesarean deliveries. They were divided into a low-risk (n = 149) and a high-risk (n = 116) group according to predefined risk factors for puerperal uterine complications. The ultrasonographic findings were dichotomized into no masses (endometrial strip, endometrial fluid, or hyperechoic foci) or a definite intrauterine echogenic/heterogeneous mass (IUM, > 15 mm in diameter). Results: The presence of risk factor(s) was significantly associated with uterine subinvolution, IUM, heavy delayed postpartum hemorrhage (PPH), and a need for uterine curettage. Multivariable logistic regression analysis for the risk factor(s) that can predict the occurrence of heavy delayed PPH showed that the presence of an IUM was the most predictive variable. The presence of an IUM and heavy delayed PPH predicted uterine curettage in 61.3% and 37.5% of patients, respectively. Conclusion: Routine uterine scanning on Day 1 and Day 14 postpartum is an easy, inexpensive, valuable method that can be offered to women at high risk for delayed PPH due to subinvolution or the presence of an IUM. Accordingly, it may be predicted which women will benefit from uterine curettage in up to two-thirds of cases.

Federation of Gynecology and Obstetrics.
AU - Shaamash, A. H.
AU - Ahmed, A. G.M.
AU - Abdel Latef, M. M.
AU - Abdullah, S. A.
DO - 10.1016/j.ijgo.2007.03.042
IS - 2
KW - Prediction
KW - Puerperal uterine complications
KW - Routine postpartum ultrasonography
PB - John Wiley and Sons Ltd
PY - 2007
SP - 93
EP - 99
TI - Routine postpartum ultrasonography in the prediction of puerperal uterine complications
T2 - International Journal of Gynecology and Obstetrics
VL - 98
ER -
TY - JOUR
AB - Aims: To assess the appearance of the post-partum uterus on transabdominal ultrasound, and to correlate these findings with maternal morbidity. Methods: In a prospective observational study, 94 women were seen within 24 h of their delivery and assessed by transabdominal ultrasound. Volumetric data were calculated from measurements of intrauterine echogenic areas. All women were contacted for a telephone interview 1-4 months following their delivery to assess whether they had experienced morbidity associated with their delivery such as post-partum haemorrhage, pyrexia, prolonged hospital stay, follow-up investigations or surgical intervention. Results: Two areas of echogenic material were identified in the upper and lower segment of the post-partum uterus. These were assessed independently for dimensions and volumes. The upper segment area had an average thickness of 13.8 mm and an average volume of 35.6 cm3 The lower segment/cervical area held considerably more material with an average volume of 54.8 cm3. The mean duration of post-partum bleeding was 4.2 weeks. None of the recruited women required a blood transfusion. The average hospital stay was 4 days. Twenty-two (23%) of the participants experienced a febrile illness following delivery, and 19 (20%) were commenced on antibiotics. None of these parameters of post-partum morbidity were associated with the ultrasound findings. Conclusions: In this study ultrasound evaluation in the immediate post-partum period revealed unexpectedly large volumes of echogenic material in the uterine cavity. However, such volumes of echogenic material were not associated with postnatal morbidity, and can probably be accepted as normal. © 2006 The Authors Journal compilation © 2006 The Royal Australian and New Zealand College of Obstetricians and Gynaecologists.
AU - Deans, Rebecca
AU - Dietz, Hans Peter
DA - 2006/8//
DO - 10.1111/j.1479-828X.2006.00604.x
IS - 4
KW - Haemorrhage
KW - Morbidity

KW - Post-partum
KW - Transabdominal ultrasound
KW - Uterus
PY - 2006
SP - 345
EP - 349
TI - Ultrasound of the post-partum uterus
T2 - Australian and New Zealand Journal of Obstetrics and Gynaecology
VL - 46
ER -
TY - JOUR
AB - Objective: To establish normal ultrasonographic findings for the postpartum uterus after vaginal delivery, and to characterize associated bleeding patterns. Methods: Postpartum women were scanned by transabdominal ultrasound within 48 h after normal vaginal delivery. Uterine length, uterine width, endometrial stripe thickness and endometrial contents were evaluated by a single sonographer. Patients maintained a daily symptom diary for 6 weeks and were interviewed by telephone at 2 weeks. Statistical analysis was performed using χ2, Fisher's exact test, Student's t test and Pearson correlation. Results: Mean endometrial stripe thickness was 1.1 ± 0.6 cm, mean uterine length was 16.1 ± 1.7 cm and mean uterine width was 8.7 ± 1.0 cm. Postpartum bleeding requiring more than four protective pads per day for ≥ 10 days was associated with a thicker endometrial stripe (1.5 ± 0.7 cm vs. 0.9 ± 0.4 cm, p = 0.006). However, no patients experienced postpartum bleeding complications requiring intervention. Of the 40 women evaluated, 16 had echogenic material in the uterine cavity (mean size 12.7 ± 6.9 cm2). The presence of echogenic material was not associated with the amount or duration of bleeding. Conclusions: Frequent postpartum ultrasonographic findings include a thickened endometrial stripe and echogenic material in the uterine cavity. The echogenic material commonly seen in the endometrial cavity of asymptomatic patients was not associated with the development of bleeding complications.
AU - Sokol, E. R.
AU - Casele, H.
AU - Haney, E. I.
DA - 2004/2//
DO - 10.1080/14767050310001650798
IS - 2
KW - Echogenic material
KW - Postpartum bleeding
KW - Postpartum ultrasound
KW - Uterine cavity
KW - Uterus
PY - 2004
SP - 95
EP - 99
TI - Ultrasound examination of the postpartum uterus: What is normal?
T2 - Journal of Maternal-Fetal and Neonatal Medicine
VL - 15
ER -
TY - JOUR
AB - Objective: The purpose of this study is to analyze uterine electromyography

burst patterns in patients with spontaneous labor and patients with uterine inertia. Materials and methods: Uterine electromyography was recorded using 4 silver/silver chloride electrodes placed periumbilical. Thirty women in the spontaneous labor were enrolled. Uterine electromyography was also recorded from patients with uterine inertia before and after oxytocin treatment. EMG bursts were characterized by analysis of multiple variables including burst frequency, duration, root mean squared, amplitude, and total power. Results: There were significant reductions (P <.01) in all EMG burst characteristics. In addition, uterine electromyography parameters were all increased after oxytocin treatment and were comparable (P >.05) to patients in spontaneous labor. Conclusions: Uterine electromyography can be used effectively to distinguish patients progressing with spontaneous labor from patients that develop uterine inertia. Uterine inertia is characterized by reduced EMG activity and failure of cervical dilation. Uterine electromyography is a quantitative, non-invasive assessment tool that contributes to the diagnosis, evaluation and management of patients with spontaneous labor and uterine inertia.
AU - Li, Pin
AU - Wang, Lele
AU - Qian, Xueya
AU - Morse, Abraham
AU - Garfield, Robert E.
AU - Liu, Huishu
DA - 2021/5//
DO - 10.1016/j.tjog.2021.03.010
IS - 3
KW - Cervical dilation
KW - Oxytocin
KW - Uterine contractions
KW - Uterine electromyography
KW - Uterine inertia
PB - Elsevier Ltd
PY - 2021
SP - 449
EP - 453
TI - A study of uterine inertia on the spontaneous of labor using uterine electromyography
T2 - Taiwanese Journal of Obstetrics and Gynecology
VL - 60
ER -
TY - JOUR
AB - Objectives: To define the ultrasonographic appearance of the uterus and the uterine cavity, including its contents, in normal women making an uncomplicated postpartum recovery. Methods: Forty women were scanned on days 7, 14, and 21 postpartum. At each scan the uterine and cavity volumes were estimated, and the appearance of the uterine cavity contents was documented. The amount and duration of postpartum vaginal bleeding, and method of infant feeding were also recorded. Results: The mean duration of postpartum bleeding was 24.5 (range 14-45.) days. Fifty-one percent (95% confidence interval 34-68) of the subjects scanned at 7 days postpartum, 21%(8-36) at 14 days, and 6%(0.8-20) at 21 days, had an echogenic mass within the uterine cavity. Statistical analysis revealed no difference, in terms of

bleeding duration, between women with a uterine cavity echogenic mass noted at 7, 14, or 21 days postpartum, and those without (unpaired t-test, P = 0.42, 0.39, and 0.06). The presence of an echogenic mass was not associated with heavier bleeding at the time of any of the scans (chi-squared test, P = 0.58, 0.56, and 0.28). Statistical analysis revealed no correlation between the duration or amount of bleeding, and the uterine or cavity volume, at any of the three scans. Conclusion: In this study, ultrasound evaluation of the uterine cavity revealed an echogenic mass in 51% of women with normal postpartum bleeding at 7 days, 21% at 14 days, and 6% at 21 days postpartum. This questions the significance of echogenic material within the uterine cavity in the postpartum period.
AU - Edwards, Dr A.
AU - Ellwood, D. A.
DO - 10.1046/j.1469-0705.2000.00234.x
IS - 7
KW - Curettage
KW - Hemorrhage
KW - Involution
KW - Postpartum
KW - Uterine cavity
KW - Uterus
PY - 2000
SP - 640
EP - 643
TI - Ultrasonographic evaluation of the postpartum uterus
T2 - Ultrasound in Obstetrics and Gynecology
VL - 16
ER -
TY - RPRT
AB - Objectives To define the ultrasonographic appearance of the uterus and the uterine cavity, including its contents, in normal women making an uncomplicated postpartum recovery. Methods Forty women were scanned on days 7, 14, and 21 postpartum. At each scan the uterine and cavity volumes were estimated, and the appearance of the uterine cavity contents was documented. The amount and duration of postpartum vaginal bleeding, and method of infant feeding were also recorded. Results The mean duration of postpartum bleeding was 24.5 (range 14±45) days. Fifty-one percent (95% confidence interval 34±68) of the subjects scanned at 7 days postpartum, 21%(8±36) at 14 days, and 6%(0.8±20) at 21 days, had an echogenic mass within the uterine cavity. Statistical analysis revealed no difference, in terms of bleeding duration, between women with a uterine cavity echogenic mass noted at 7, 14, or 21 days postpartum, and those without (unpaired t-test, P 0.42, 0.39, and 0.06). The presence of an echogenic mass was not associated with heavier bleeding at the time of any of the scans (chi-squared test, P 0.58, 0.56, and 0.28). Statistical analysis revealed no correlation between the duration or amount of bleeding, and the uterine or cavity volume, at any of the three scans. Conclusion In this study, ultrasound evaluation of the uterine cavity revealed an echogenic mass in 51% of women with normal postpartum bleeding at 7 days, 21% at 14 days, and 6% at 21 days postpartum. This questions the significance of echogenic material within the uterine cavity in the postpartum period.
AU - Edwards, A
AU - Ellwood, D A

KW - Curettage
KW - Hemorrhage
KW - Involution
KW - Postpartum
KW - Uterine cavity
KW - Uterus
PY - 2000
SP - 640
EP - 643
TI - Ultrasonographic evaluation of the postpartum uterus
T2 - Ultrasound Obstet Gynecol
VL - 16
ER -
TY - JOUR
AB - This article describes the variable appearance of the normal postpartum uterus and reviews complications which can occur in the postpartum period, with particular emphasis on the sonographic findings. Postpartum complications are a common presentation to the emergency department. The majority of these patients present with secondary postpartum hemorrhage. Additional symptoms of pain or clinical findings of pyrexia and leukocytosis confound the clinical scenario and necessitate further evaluation with imaging. Ultrasonography is the mainstay in the initial imaging evaluation of the postpartum patient, with occasional progression to CT, MR, or angiography. We sought to provide a brief review of the literature, with pictorial review of key imaging findings, with a focus on ultrasonography. We provide a pictorial and brief literature review, with case examples from our institution, of key postpartum complications. Ultrasonography is an important component of evaluation in postpartum patients, particularly those with hemorrhage or other complication.
AU - Kostrubiak, Danielle (Kruse)
AU - DeHay, Price W.
AU - Akselrod, Dmitriy G.
AU - D’Agostino, Robert
AU - Tam, Judy K.
DA - 2021/8//
DO - 10.1007/s10140-021-01927-0
IS - 4
KW - Cesarean section
KW - Complications
KW - Postpartum
KW - Ultrasonography
PB - Springer Science and Business Media Deutschland GmbH
PY - 2021
SP - 857
EP - 862
TI - Emergent postpartum pelvic sonography
T2 - Emergency Radiology
VL - 28
ER -
TY - JOUR
AU - Ucci, Matteo Antonio

AU - Mascio, Daniele Di
AU - Bellussi, Federica
AU - Berghella, Vincenzo
DO - 10.1016/j
PY - 2021
TI - Ultrasound evaluation of the uterus in the uncomplicated postpartum period: a systematic review
UR - http://dx.doi.org/10.1016/j.
ER -
TY - JOUR
AB - Postpartum hemorrhage is a leading cause of maternal mortality. Various methods can be used to evaluate the postpartum uterine cavity volume. This work aims to introduce a simple method for uterine postpartum cavity volume evaluation, called Postpartum Uterine Ultrasonographic Scale (PUUS), which could be used routinely. In this prospective study, 131 consecutive Caucasian patients were evaluated by using the PUUS method. The mean age was 27.72 years (ranging from 15 to 42). Patients were examined in the same time intervals: within the first 24-48 hours after delivery in case of vaginal delivery, and within the first 48-72 hours, in case of cesarean delivery. Patients with PUUS grades 2, 3, or 4 were reexamined daily until the PUUS grade declined to 1 or 0. The PUUS method evaluated the length of the endometrium of the uterine cavity occupied by blood or debris, from grade 0 (no blood) to grade 4 (over three-quarters of the endometrial length occupied by blood/debris). The PUUS grade of uterine involution varied with the day of examination, gestation, and parity. In this article, a novel method of evaluating uterine postpartum involution titled PUUS is introduced. This method standardized uterine cavity involution in a numerical fashion. We hope that the PUUS scale could further be used to decrease the morbidity and mortality of women due to postpartum hemorrhage.
AU - Covali, Roxana
AU - Socolov, Demetra
AU - Socolov, Razvan Vladimir
AU - Akad, Mona
DO - 10.25122/jml-2020-0107
IS - 4
KW - endometrial length
KW - obstetric delivery
KW - postpartum hemorrhage
KW - uterine retraction
KW - uterine ultrasonography
PB - Carol Davila University Press
PY - 2021
SP - 511
EP - 517
TI - Postpartum Uterine Ultrasonographic Scale: a novel method to standardize the assessment of uterine postpartum involution
T2 - Journal of Medicine and Life
VL - 14
ER -
TY - JOUR
AB - The aim of this study was to estimate the efficacy of contrast-enhanced

ultrasound (CEUS) in detecting postpartum hemorrhage (PPH) after cesarean section. This is the first study of CEUS in obstetric hemorrhage. A total of 37 patients, operated at Nagoya University Hospital, underwent CEUS. We evaluated the findings of CEUS, which were qualitatively defined as positive when pooling or leakage of contrast agent was observed in the uterine cavity, by measuring the amount of bleeding during the first 4 h after cesarean section. The time–intensity curve patterns of leaked contrast agents were also analyzed for quantitative prediction of the amount of blood loss. Significant differences between the excessive hemorrhage (N = 7) and non-excessive hemorrhage groups (N = 30) were noted in the occurrence of positive CEUS (p = 0.011). Additionally, mean postpartum blood loss markedly increased in patients with a positive CEUS (p = 0.002). From a quantitative perspective, the time until leakage of contrast agents was detected correlated with the amount of bleeding, but the other characteristics of the time–intensity curve pattern did not provide valuable information. In conclusion, CEUS, which enables bedside assessment and rapid diagnosis, is a promising strategy for the detection of PPH.
AU - Imai, Kenji
AU - Kotani, Tomomi
AU - Tsuda, Hiroyuki
AU - Nakano, Tomoko
AU - Hirakawa, Akihiro
AU - Kikkawa, Fumitaka
DA - 2017/3//
DO - 10.1016/j.ultrasmedbio.2016.11.008
IS - 3
KW - Cesarean section
KW - Contrast-enhanced ultrasound
KW - Obstetrics
KW - Perflubutane
KW - Postpartum hemorrhage
PB - Elsevier USA
PY - 2017
SP - 615
EP - 620
TI - A Novel Approach to Detecting Postpartum Hemorrhage Using Contrast-Enhanced Ultrasound
T2 - Ultrasound in Medicine and Biology
VL - 43
ER -
TY - JOUR
AB - Uterine artery pseudoaneurysm (UAP) rupture should be considered in case of late genital bleeding without obvious cause and lead to perform a sonographic examination with Doppler-scan. We report two cases of late post-partum hemorrhage from UAP diagnosed as such using color Doppler US. In order to avert life-threatening bleeding, prompt and accurate diagnosis should be made using color Doppler US since the latter plays a significant role in demonstrating the vascular nature of this anechoic uterine lesion.
AU - Karmous, Narjes
AU - Ayachi, Amira
AU - Derouich, Sadok

AU - Mkaouar, Lassaad
AU - Mourali, Mechaal
DO - 10.11604/pamj.2016.25.136.10676
KW - Postpartum hemorrhage
KW - cesarean delivery
KW - transcatheter arterial embolization
KW - uterine artery pseudoaneurysm
PY - 2016
SP - 136
EP - 136
TI - Rupture of uterine artery pseudoaneurysm: role of ultrasonography in postpartum hemorrhage management
T2 - The Pan African medical journal
VL - 25
ER -
TY - JOUR
AB - The ability of ultrasound to predict postpartum hemorrhage remains poorly described. The aim of this study was to evaluate whether ultrasound measurement of intrauterine content can predict blood loss and postpartum hemorrhage after vaginal delivery. We used a preliminary prospective monocentric study of 201 women who delivered vaginally after 34 wk of gestation. Measurements were performed 30–45 min after normal vaginal delivery according to strict ultrasonographic criteria. Analysis of the relationship between ultrasound measurements and hemoglobin loss showed a strong linear correlation (R^2 = 0.59 and R^2 = 0.4 for isthmic and fundal measurements). The maximal value between the fundal and isthmic measurements seems to provide the best accuracy to predict loss of hemoglobin higher than 3 g/dL (area under the curve [AUC] of the receiver operating characteristic curve, 0.9; 95% confidence interval [CI], [0.76–0.97]) and post-partum hemorrhage (AUC, 0.99; 95%CI, [0.984–0.99]). In case of intrauterine content >2 cm (135/201), the risks of loss of hemoglobin higher than 3 g/dL (5/135 vs. 0/66) and post-partum hemorrhage (11/135 vs. 0/66) were increased, all the more if the intrauterine content was >4 cm (4/16 and 11/16, respectively). Considering the maximal measurement, the most optimal cut-off value for clinical practice could be 2.4 cm (sensibility 100%, specificity 57%) and 4.1 cm (sensibility 100%, specificity 97%) for loss of hemoglobin higher than 3 g/dL and post-partum hemorrhage, respectively.
AU - Hcini, Najeh
AU - Mchirgui, Ali
AU - Pomar, Léo
AU - Beneteau, Samuel
AU - Lambert, Véronique
AU - Carles, Gabriel
DA - 2020/11//
DO - 10.1016/j.ultrasmedbio.2020.07.017
IS - 11
KW - Anemia
KW - Postpartum hemorrhage
KW - Ultrasonography
PB - Elsevier Inc.
PY - 2020
SP - 3145

EP - 3153
TI - Early Prediction of Blood Loss and Postpartum Hemorrhage after Vaginal Delivery by Ultrasound Measurement of Intrauterine Content
T2 - Ultrasound in Medicine and Biology
VL - 46
ER -
TY - CONF
AB - Objective The purpose of this study was to analyze the potential of abdominopelvic ultrasonography at the initial examination in women with severe postpartum hemorrhage. Study Design One hundred twenty-five women were included in the study. The therapeutic approaches that were performed to stop the bleeding were evaluated for each category of ultrasonographic finding. Results Seventy-one women (56.8%) had normal ultrasonography; 30 women (24%) had echogenic endometrial lining; 17 women (13.6%) had echogenic intrauterine mass, and 7 women (5.6%) had abdominopelvic free fluid effusion. Medical therapies allowed the bleeding to stop in 90.1% of women with normal ultrasonography, in 66.6% of women with echogenic endometrial lining, and in 29.4% of women with echogenic intrauterine mass. Pelvic embolization and surgery were performed less frequently in women who had normal ultrasonography results (9.9%) than in women with abnormal ultrasonography results (46.8%; P < .0001). Conclusion A normal abdominopelvic ultrasonography is associated with a favorable outcome and can be considered to be a predictor for the effectiveness of conservative, noninvasive therapeutic approaches.
AU - Lousquy, Ruben
AU - Morel, Olivier
AU - Soyer, Philippe
AU - Malartic, Cécile
AU - Gayat, Etienne
AU - Barranger, Emmanuel
DO - 10.1016/j.ajog.2010.10.003
IS - 3
KW - abdominopelvic ultrasonography
KW - pelvic embolization
KW - postpartum hemorrhage
KW - surgery
PB - Mosby Inc.
PY - 2011
SP - 232.e1
EP - 232.e6
TI - Routine use of abdominopelvic ultrasonography in severe postpartum hemorrhage: Retrospective evaluation in 125 patients
T2 - American Journal of Obstetrics and Gynecology
VL - 204
ER -
TY - GEN
AB - Secondary postpartum hemorrhage (PPH) and postabortion hemorrhage are rare complications. Retained products of conception (RPOC) is among the most common causes of both secondary PPH and postabortion hemorrhage. Other less common causes of secondary PPH are uterine vascular abnormalities such as arteriovenous malformations and pseudoaneurysms. These are usually related to a history of a

procedure such as dilation and curettage or cesarean delivery. Subinvolution of the placental site is an idiopathic cause of secondary PPH; this condition may be underrecognized and therefore could have a higher incidence than currently reported. Gestational trophoblastic disease is rare but commonly presents as secondary PPH and resembles RPOC in radiologic appearance. The first-line imaging modality for secondary PPH is ultrasound, but computed tomography and magnetic resonance imaging may be used if the ultrasound findings are indeterminate. Angiography is an important tool for the definitive diagnosis of uterine vascular abnormalities. Appropriate management requires radiologists to be familiar with the multimodality imaging features of secondary PPH or postabortion hemorrhage.
AU - Iraha, Yuko
AU - Okada, Masahiro
AU - Toguchi, Masafumi
AU - Azama, Kimei
AU - Mekaru, Keiko
AU - Kinjo, Tadatsugu
AU - Kudaka, Wataru
AU - Aoki, Yoichi
AU - Aoyama, Hajime
AU - Matsuzaki, Akiko
AU - Murayama, Sadayuki
DA - 2018/1//
DO - 10.1007/s11604-017-0687-y
IS - 1
KW - Postabortion hemorrhage
KW - Postpartum hemorrhage
KW - Retained products of conception
KW - Subinvolution of the placental site
KW - Uterine vascular malformation
PB - Springer Tokyo
PY - 2018
SP - 12
EP - 22
TI - Multimodality imaging in secondary postpartum or postabortion hemorrhage: retained products of conception and related conditions
T2 - Japanese Journal of Radiology
VL - 36
ER -
TY - JOUR
AU - Escobar, Maria Fernanda
AU - Nassar, Anwar H.
AU - Theron, Gerhard
AU - Barnea, Eythan R.
AU - Nicholson, Wanda
AU - Ramasauskaite, Diana
AU - Lloyd, Isabel
AU - Chandraharan, Edwin
AU - Miller, Suellen
AU - Burke, Thomas
AU - Ossanan, Gabriel

AU - Andres Carvajal, Javier
AU - Ramos, Isabella
AU - Hincapie, Maria Antonia
AU - Loaiza, Sara
AU - Nasner, Daniela
AU - Nassar, Anwar H.
AU - Visser, Gerard H.
AU - Barnea, Eytan R.
AU - Escobar, Maria Fernanda
AU - Kim, Yoon Ha
AU - Nicholson, Wanda Kay
AU - Pacagnella, Rodolfo
AU - Ramasauskaite, Diana
AU - Theron, Gerhard
AU - Wright, Alison
DA - 2022/3//
DO - 10.1002/ijgo.14116
IS - S1
KW - FIGO recommendations
KW - PPH
KW - PPH prevention
KW - PPH treatment
KW - management
KW - postpartum hemorrhage
PB - John Wiley and Sons Ltd
PY - 2022
SP - 3
EP - 50
TI - FIGO recommendations on the management of postpartum hemorrhage 2022
T2 - International Journal of Gynecology and Obstetrics
VL - 157
ER -
TY - GEN
AB - Postpartum hemorrhage (PPH) is a potentially life threatening condition, and it remains the leading cause of maternal morbidity. Uterine atony, lower genital tract lacerations, uterine rupture or inversion, retained products of conception and underlying coagulopathy are some of the common causes of PPH. Most conditions can be diagnosed based on clinical and laboratory evaluation supplemented by ultrasound information. Computed tomography (CT) or magnetic resonance (MR) imaging can provide information for the detection, localization and characterization of PPH in some difficult cases. CT can accurately demonstrate the anatomic location of significant arterial hemorrhage as sites of intravenous contrast material extravasation, which can be as a guide for angiographic intervention. The presence of focal or diffuse intravenous contrast extravasation or a hematoma within the enlarged postpartum uterine cavity on CT can help the diagnosis of uterine atony when the clinical diagnosis of uterine atony is unclear. CT can also provide the information of other alternative conditions such as a puerperal genital hematoma, uterine rupture and concealed hematoma in other sites. MR imaging may be considered as a valuable complement to ultrasound where the ultrasound findings are inconclusive in the diagnosis and differential diagnosis of retained products of

conception. Knowledge of the various radiologic appearances of PPH and the correlation with clinical information can ensure correct diagnosis and appropriate and prompt treatment planning in the patients with PPH.
AU - Lee, Nam Kyung
AU - Kim, Suk
AU - Lee, Jun Woo
AU - Sol, Yu Li
AU - Kim, Chang Won
AU - Hyun Sung, Kim
AU - Jang, Ho Jin
AU - Suh, Dong Soo
DA - 2010/4//
DO - 10.1016/j.ejrad.2009.04.062
IS - 1
KW - CT
KW - Complications
KW - Hemorrhage
KW - MR
KW - Pregnancy
KW - Uterus
PY - 2010
SP - 50
EP - 59
TI - Postpartum hemorrhage: Clinical and radiologic aspects
T2 - European Journal of Radiology
VL - 74
ER -
TY - JOUR
AB - Pelvic pain and vaginal bleeding are common symptoms in postpartum women presenting to the emergency room (ER). Pelvic ultrasonography plays a crucial role in evaluating symptomatic postpartum patients by allowing a rapid diagnosis and treatment initiation. The main goal of imaging is to distinguish between causes of pelvic pain and vaginal bleeding that may be managed conservatively and those requiring emergent intervention. This pictural essay focuses on the ultrasonographic features of common postpartum conditions for which patients may present to the ER with vaginal bleeding and pelvic pain, including retained products of conception, endometritis, uterine arteriovenous malformation, uterine artery pseudoaneurysm, ovarian vein thrombosis, bladder flap hematoma, and uterine dehiscence/rupture.
AU - Vardar, Zeynep
AU - Dupuis, Carolyn S.
AU - Goldstein, Alan J.
AU - Siddiqui, Efaza
AU - Vardar, Baran Umut
AU - Kim, Young H.
DA - 2022/10//
DO - 10.14366/usg.22004
IS - 4
KW - Emergency

KW - Postpartum
KW - Radiology
KW - Transvaginal
KW - Ultrasonography
PB - Korean Society of Ultrasound in Medicine
PY - 2022
SP - 782
EP - 795
TI - Pelvic ultrasonography of the postpartum uterus in patients presenting to the emergency room with vaginal bleeding and pelvic pain
T2 - Ultrasonography
VL - 41
ER -
TY - JOUR
AB - We evaluated normal uterine involution prospectively with real-time ultrasonography in 100 women after uncomplicated term vaginal delivery. Transducers easily distorted the spongy uterus during early postpartum scanning, an effect minimized with sector transducers that are superior to linear or convex probes for accurate early postpartum uterine measurement. Long-axis measurements correcting for uterine angulation were the most reproducible and accurate, irrespective of bladder distention. Uterine T o our knowledge, only three studies have addressed ultrasonographic measurement of normal postpartum uterine dimensions. 1-J Since only static scanners were utilized in these studies , the reported dimensions bear uncertain relevance to real~ time ultrasonography owing to two factors: (1) The long axis of the postpartum uterus often is oriented obliquely rather than parallel to the sagittal plane of the body." Imaging in standard orthogonal planes may therefore underestimate the true sagittal uterine dimension. (2) Our initial real-time ultrasono-graphic observations indicated that the early postpar
AU - Wachsberg, Ronald H
AU - Kurtz, Alfred B
AU - Levine, Charles O
AU - Solomon, Philip
AU - Wapner, Ronald J
AU - Gynecology, and PS
PY - 2014
SP - 215
EP - 221
TI - Real-Time Ultrasonographic Analysis of the Normal Postpartum Uterus: Technique, Variability, and Measurements
T2 - J Ultrasound Med
VL - 13
ER -
TY - RPRT
AB - Maternal hemorrhage, defined as a cumulative blood loss of greater than or equal to 1,000 mL or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after the birth process, remains the leading cause of maternal mortality worldwide (1). Additional important secondary sequelae from hemorrhage exist and include adult respiratory distress syndrome, shock, disseminated intravascular coagulation, acute renal failure, loss of fertility, and pituitary necrosis (Sheehan syndrome). Hemorrhage that leads to blood transfusion is the

leading cause of severe maternal morbidity in the United States closely followed by disseminated intravascular coagulation (2). In the United States, the rate of postpartum hemorrhage increased 26% between 1994 and 2006 primarily because of increased rates of atony (3). In contrast, maternal mortality from postpartum obstetric hemorrhage has decreased since the late 1980s and accounted for slightly more than 10% of maternal mortalities (approximately 1.7 deaths per 100,000 live births) in 2009 (2, 4). This observed decrease in mortality is associated with increasing rates of transfusion and peripartum hysterectomy (2-4). The purpose of this Practice Bulletin is to discuss the risk factors for postpartum hemorrhage as well as its evaluation , prevention, and management. In addition, this document will encourage obstetrician-gynecologists and other obstetric care providers to play key roles in implementing standardized bundles of care (eg, policies, guidelines, and algorithms) for the management of postpartum hemorrhage.
AU - Shields Laurence E.
AU - Goffman Dena
AU - Caughey Aaron B.
PY - 2017
SP - 168
EP - 186
TI - Committee on Practice Bulletins-Obstetrics. Practice Bulletin No. 183: Postpartum Hemorrhage. Obstet Gynecol
UR - http://www1.health.nsw.gov.au/pds/ActivePDSDocuments/
ER -
TY - JOUR
AB - Postpartum hemorrhage is a leading cause of maternal mortality. Various methods can be used to evaluate the postpartum uterine cavity volume. This work aims to introduce a simple method for uterine postpartum cavity volume evaluation, called Postpartum Uterine Ultrasonographic Scale (PUUS), which could be used routinely. In this prospective study, 131 consecutive Caucasian patients were evaluated by using the PUUS method. The mean age was 27.72 years (ranging from 15 to 42). Patients were examined in the same time intervals: within the first 24-48 hours after delivery in case of vaginal delivery, and within the first 48-72 hours, in case of cesarean delivery. Patients with PUUS grades 2, 3, or 4 were reexamined daily until the PUUS grade declined to 1 or 0. The PUUS method evaluated the length of the endometrium of the uterine cavity occupied by blood or debris, from grade 0 (no blood) to grade 4 (over three-quarters of the endometrial length occupied by blood/debris). The PUUS grade of uterine involution varied with the day of examination, gestation, and parity. In this article, a novel method of evaluating uterine postpartum involution titled PUUS is introduced. This method standardized uterine cavity involution in a numerical fashion. We hope that the PUUS scale could further be used to decrease the morbidity and mortality of women due to postpartum hemorrhage.
AU - Covali, Roxana
AU - Socolov, Demetra
AU - Socolov, Razvan Vladimir
AU - Akad, Mona
DO - 10.25122/jml-2020-0107
IS - 4
KW - endometrial length
KW - obstetric delivery

KW - postpartum hemorrhage
KW - uterine retraction
KW - uterine ultrasonography
PB - Carol Davila University Press
PY - 2021
SP - 511
EP - 517
TI - Postpartum Uterine Ultrasonographic Scale: a novel method to standardize the assessment of uterine postpartum involution
T2 - Journal of Medicine and Life
VL - 14
ER -
TY - JOUR
AU - Ucci, Matteo Antonio
AU - Mascio, Daniele Di
AU - Bellussi, Federica
AU - Berghella, Vincenzo
DO - 10.1016/j
PY - 2021
TI - Ultrasound evaluation of the uterus in the uncomplicated postpartum period: a systematic review
UR - http://dx.doi.org/10.1016/j.
ER -
TY - JOUR
AB - Background: Uterine involution assessments are critical for the prevention of postpartum hemorrhage. Various methods have been used worldwide. Methods: The PUUS (Postpartum Uterine Ultrasonographic Scale) method evaluates, by transabdominal ultrasonography, the length of the endometrium of the uterine cavity occupied by blood or debris, from grade 0 (no blood) to grade 4 (over three-quarters of the endometrial length occupied by blood/debris). A total of 131 consecutive patients admitted for delivery in the Elena Doamna Obstetrics and Gynecology University Hospital in Iasi, Romania, were prospectively evaluated using the PUUS method. The mean age was 27.72 years old, and they were examined during the first 24–48 h after vaginal delivery, or in the first 48–72 h after cesarean delivery. For patients with a PUUS grade greater than 1, re-examination was preformed daily in the following days, until the PUUS grade decreased to 1 or 0. Results: By standardizing uterine involution in a numerical fashion, we precisely demonstrate that uterine involution varied with the method of delivery (vaginal/cesarean) and with the number of vials of oxytocin received intrapartum, but not with the number of vials of ergometrine maleate received, and not with the origin of the parturient (rural/urban).
AU - Covali, Roxana
AU - Socolov, Demetra
AU - Carauleanu, Alexandru
AU - Pavaleanu, Ioana
AU - Akad, Mona
AU - Boiculese, Lucian Vasile
AU - Socolov, Razvan Vladimir
DA - 2021/9//
DO - 10.3390/diagnostics11091731

IS - 9
KW - Endometrial length
KW - Obstetric delivery
KW - Postpartum hemorrhage
KW - Uterine retraction
KW - Uterine ultrasonography
PB - Multidisciplinary Digital Publishing Institute (MDPI)
PY - 2021
TI - The importance of the novel postpartum uterine ultrasonographic scale in numerical assessments of uterine involution regarding perinatal maternal and fetal outcomes
T2 - Diagnostics
VL - 11
ER -
TY - JOUR
AB - Purpose: The purpose of this study is to compare uterine sonographic characteristics in early puerperium, following vaginal versus cesarean deliveries; and in women with abnormal third stage of labor, compared to uncomplicated vaginal delivery. Materials and methods: This is a prospective study of women after delivery of singleton, appropriate-for-gestational-age weight, term neonates; 66 women delivered vaginally and 33 delivered by cesarean section. Sonographic uterine dimensions (height, length, and width), intracavitary thickness and its echogenicity (at level of fundus, midcavity and cervix) were recorded at less than and after 24 h from delivery, and compared between women delivered vaginally and by cesarean section. Among women delivered vaginally, data were further analyzed according to whether women underwent manual revision of the uterine cavity. Results: Sonographic evaluations were taken at 15.4 (4.3–24.0) and 39.5 (28.8–108.8) hours after delivery (median, range). We found no clinically significant differences in uterine characteristics according to mode of delivery or according to manual revision of the uterine cavity. The sonographic appearance of the uterus was similar when performed at less than or after 24 h from delivery. Conclusions: Postpartum sonographic evaluation of the uterus appears similar after vaginal and cesarean deliveries.
AU - Bardin, Ron
AU - Ashwal, Eran
AU - Zilber, Hila
AU - Tenenbaum-Gavish, Kinneret
AU - Hiersch, Liran
AU - Hadar, Eran
AU - Meizner, Israel
AU - Gabbay-Benziv, Rinat
DA - 2018/8//
DO - 10.1080/14767058.2017.1333099
IS - 15
KW - Postpartum
KW - cesarean section
KW - sonographic characteristics
KW - uterine cavity
KW - vaginal delivery
PB - Taylor and Francis Ltd

PY - 2018
SP - 1983
EP - 1988
TI - Sonographic appearance of the uterus in the early puerperium in vaginal versus cesarean deliveries: a prospective study
T2 - Journal of Maternal-Fetal and Neonatal Medicine
VL - 31
ER -
TY - RPRT
AB - The ultrasound findings in the postpartum uterus will be described with a focus on differentiating normal from pathologic conditions. Imaging of the postpartum uterus will include a discussion of the normal postpartum uterus, postpartum hematomas, and retained products of conception. Clinical management and therapeutic implications based on sonographic findings will be emphasized.
AU - Steinkeler, Jill
AU - Coldwell, Bobbi-Jo
AU - Warner, Mary A
KW - bladder flap hematoma
KW - postpartum uterus
KW - retained products of conception (Ultrasound Quarterly 2012;28:97Y103)
KW - subfascial hematoma
PY - 2012
TI - Ultrasound of the Postpartum Uterus
UR - www.ultrasound-quarterly.com
ER -
TY - JOUR
AB - Objectives: To evaluate the color Doppler and gray-scale sonographic appearance of the uterus after pregnancy, with special attention to the occurrence of areas of enhanced vascularity and placental remnants. Patients and methods: Cross-sectional observational study involving 385 consecutive women presenting at their first visit after pregnancy. The uterus was evaluated using ultrasound with color Doppler. In the presence of placental remnants, blood was sampled for measurement of beta human chorionic gonadotropin (βhCG), hemoglobin (Hb)and infectious parameters. If indicated, a dilatation and curettage was performed. Results: In 8.3% of women, areas of enhanced vascularity were detected with color Doppler examination. Most cases (68.9%) were focal areas of one or more vessels. In 2.6% of patients abnormal vascularity extended over a large area of the whole myometrium. In 6.75% of cases, placental remnants were detected. In 46% of these, blood sampling revealed βhCG levels below 30 mIU/mL; serological infection parameters and Hb concentration were within the normal range. Conclusions: Areas of enhanced vascularity of the uterus, ranging from a focal vascular pedicle to a larger area of the myometrium, are relatively common after pregnancy. They are predominantly seen in the presence of placental remnants, in the early postpartum period and after instrumental or manual delivery of the placenta. There are no clear risk factors for retained placental tissue, besides the history of blood transfusion in the early postpartum, and perhaps multi-gravidity. Serology is of little help in the diagnosis of retained gestational products. The knowledge of the ultrasound and color Doppler features of the uterus after pregnancy may prove of practical value for the management of abnormal uterine bleeding in the postpartum period.

AU - Van den Bosch, Thierry
AU - Van Schoubroeck, D.
AU - Lu, C.
AU - De Brabanter, J.
AU - Van Huffel, S.
AU - Timmerman, D.
DO - 10.1046/j.1469-0705.2002.00851.x
IS - 6
KW - Arteriovenous malformations
KW - Color Doppler
KW - Placental remnants
KW - Postpartum
KW - Ultrasound
PY - 2002
SP - 586
EP - 591
TI - Color Doppler and gray-scale ultrasound evaluation of the postpartum uterus
T2 - Ultrasound in Obstetrics and Gynecology
VL - 20
ER -
TY - JOUR
AB - Purpose. To examine the uterine involution period after uncomplicated delivery in primiparous and multiparous women. Methods. Longitudinal prospective study. Repeated parameters were measured and endometrial contents and diastolic notch were observed. Measurements of primiparous and multiparous women were carried out after labour on the 1st, 3rd, 10th, 30th, 42nd, and 60th postpartum days. The analysis was performed using SPSS version 21. Results. The median uterus parameters are bigger in multiparous group in physiological puerperium, but the decreasing trend is the same. The endometrial cavity on the 10th day was significantly wider in multiparous women and mainly echo-negative view of the uterine cavity was observed. The evaluation of the uterine angle deviation changes from an extremely retroverted position to a more anteverted position. RI of the uterine artery in both groups was low immediately after labour and significantly increased one month postpartum. Notching of the uterine artery undergoes changes, but diastolic notch does not appear in all postpartum women even after two months following labour. Conclusions. The puerperium period after normal vaginal delivery depends on parity. The trend of involution in primiparous and multiparous women follows a similar pattern, yet, it lasts longer in the multiparous women. Ultrasound of uterine is certainly a useful tool after labour and may be important in facilitating an early detection of postpartum uterine complications.
AU - Paliulyte, V.
AU - Drasutiene, G. S.
AU - Ramasauskaite, D.
AU - Bartkeviciene, D.
AU - Zakareviciene, J.
AU - Kurmanavicius, J.
DO - 10.1155/2017/6739345
PB - Hindawi Limited
PY - 2017
TI - Physiological Uterine Involution in Primiparous and Multiparous Women:

Ultrasound Study
T2 - Obstetrics and Gynecology International
VL - 2017
ER -
TY - JOUR
AB - Objective. To describe uterine involution in the puerperium with three-dimensional ultrasound. Design. Prospective, longitudinal study. Setting. Fetal medicine unit, department of obstetrics and gynecology, university referral hospital, Uppsala, Sweden. Population. Fifty women with uncomplicated deliveries and puerperium between February 2009 and February 2010. Methods. Three-dimensional ultrasound was used to measure the uterine body and cavity volumes. The volume data set was analysed using virtual organ computer-aided analysis (VOCAL) with a 30 degree rotation step. Measurements were performed transabdominally on days 1, 7 and 14 and transvaginally on days 28 and 56 postpartum. Parity, gestational age, birthweight, smoking, breastfeeding and blood loss were recorded. Main outcome measures. Uterine body and cavity volumes. Results. Median uterine body volume was 756 cm3 on day 1, 440 cm3 on day 7, 253 cm3 on day 14, 125 cm3 on day 28 and 68 cm3 on day 56. Median cavity volume was 22 cm 3 on day 1, 18 cm3 on day 7, 6 cm3 on day 14, 1 cm3 on day 28 and not measurable on day 56. The interindividual variation of uterine body and cavity volumes was most pronounced on day 1 and decreased throughout the observation period. Intrauterine content was found in 36% of the women on day 1, 95% on day 7, 87% on day 14 and 28% on day 28. Conclusions. Three-dimensional ultrasound is a non-invasive tool suitable for measurement of the uterine body and cavity volumes during the puerperium. The volumes decreased in a similar pattern in the study population. © 2012 Nordic Federation of Societies of Obstetrics and Gynecology.
AU - Belachew, Johanna
AU - Axelsson, Ove
AU - Mulic-Lutvica, Ajlana
AU - Eurenius, Karin
DA - 2012/10//
DO - 10.1111/j.1600-0412.2012.01418.x
IS - 10
KW - Normal puerperium
KW - three-dimensional ultrasound
KW - uterine cavity
KW - uterus
KW - volume
PY - 2012
SP - 1184
EP - 1190
TI - Longitudinal study of the uterine body and cavity with three-dimensional ultrasonography in the puerperium
T2 - Acta Obstetricia et Gynecologica Scandinavica
VL - 91
ER -
TY - JOUR
AB - Objective: To describe uterine and uterine cavity changes throughout the puerperium, as revealed by ultrasound. Methods: This was a prospective, longitudinal study in which 42 women with uncomplicated vaginal term deliveries

were examined serially by ultrasound on postpartum days 1, 3, 7, 14, 28 and 56. The first four examinations were performed transabdominally and the last two transvaginally. The involution process of the uterus was assessed by measuring the anteroposterior diameter of the uterus and uterine cavity. Morphological findings were recorded. The influence on the involution process of parity, breast-feeding, maternal smoking and infant's birth weight were also evaluated. Results: The maximum anteroposterior diameter of the uterus diminished substantially and progressively from 92.0 mm on day 1 postpartum to 38.9 mm on day 56. The maximum anteroposterior diameter of the uterine cavity diminished from 15.8 mm on day 1 to 4.0 mm on day 56. However, the anteroposterior diameter of the uterine cavity, 5 cm from the fundus, typically increased on days 7 and 14 postpartum. The position of the uterus and the shape and the appearance of the cavity change in a unique way during the normal puerperium. The uterus was most often retroverted and empty in the early puerperium. Fluid and debris in the whole cavity were seen in the middle part of the puerperium. In late puerperium the cavity was empty and appeared as a thin white line. Endometrial gas was occasionally visualized. No correlation was found between the involution of the uterus and parity, breast-feeding and the infant's birth weight. Conclusion: Transabdominal sonography is suitable for examination of the uterus during the first 14 days postpartum but from day 28 the transvaginal route is preferable. The uterine body and position, as well as the cavity, are easy to examine by ultrasound. Accumulation of fluid and debris in the uterine cavity is a common and insignificant finding of the involuting uterus. It is located in the cervical area in the early puerperium and in the whole uterine cavity in the middle part of the puerperium. Findings from uncomplicated vaginal deliveries are needed as a reference when the diagnostic efficacy of ultrasound for pathological conditions is to be tested.
AU - Mulic-Lutvica, A.
AU - Bekuretsion, M.
AU - Bakos, O.
AU - Axelsson, O.
DO - 10.1046/j.0960-7692.2001.00561.x
IS - 5
KW - Human pregnancy
KW - Normal puerperium
KW - Ultrasound
KW - Uterus
PY - 2001
SP - 491
EP - 498
TI - Ultrasonic evaluation of the uterus and uterine cavity after normal, vaginal delivery
T2 - Ultrasound in Obstetrics and Gynecology
VL - 18
ER -
TY - JOUR
AB - Objective: To describe the biometric and morphological characteristics of the uterus through ultrasound (US) and Doppler on the uterine arteries in the initial and late puerperium after normal delivery. Methods: This was a prospective longitudinal study on full-term singleton pregnancies without complications. The patients were divided into two groups: 31 primiparous and 28 multiparous women. Two

US exams were carried out with Doppler evaluation: firstly, within the initial 48h; and secondly, between 31 and 50 days after childbirth. The US assessed the position and biometry of the uterus, appearance of the myometrium, measurement and content of the uterine cavity, and Doppler velocimetry indices of uterine arteries. To compare the groups at the two times, the paired Student t-test, Fisher's exact test and chi-square test were used. Results: In the initial puerperium, the position of the uterus was retroversion (98.3%); the appearance of the myometrium was heterogeneous (96.6%); the uterine cavity was filled with some type of material (72.9%). After the 30th day, a position was anteversion (74.6%); the appearance of the myometrium was homogeneous (91.5%); and the uterine cavity was empty (81.3%). There was an evolution in the pulsatility index between the two US exams, with an increase of 52.03% among the primiparous and 53.13% among the multiparous for the right uterine artery. Conclusion: Significant changes were observed in the morphological and biometric characteristics of the uteruses evaluated through US, as well as in the uterine arteries Doppler, between the initial and late puerperium.
AU - Diniz, Carolina Prado
AU - Júnior, Edward Araujo
AU - De Souza Lima, Marcelo Marques
AU - Guazelli, Cristina Aparecida Falbo
AU - Moron, Antonio Fernandes
DA - 2014/12//
DO - 10.3109/14767058.2014.882895
IS - 18
KW - Delivery
KW - Doppler
KW - Puerperium
KW - Ultrasound
KW - Uterus
PB - Informa Healthcare
PY - 2014
SP - 1905
EP - 1911
TI - Ultrasound and Doppler assessment of uterus during puerperium after normal delivery
T2 - Journal of Maternal-Fetal and Neonatal Medicine
VL - 27
ER -
TY - JOUR
AB - Purpose Our aim was to describe the changes observed by ultrasonography in uterine dimensions during the early puerperium among women who experienced an uncomplicated puerperium. Additionally, the influence of parity, mode of delivery, breastfeeding and birth weight on uterine involution was evaluated. Methods Ninety-one patients underwent an ultrasound examination on days 1 (D1), 2 (D2) and 7 (D7) of the postpartum period. The longitudinal, anteroposterior and transverse uterine diameters were measured, and the uterine volume was calculated by the formula: longitudinal diameter (LD) X anteroposterior diameter (APD) X transverse diameter (TD) X 0.45. The thickness and length of the uterine cavity were also measured. Results The uterine volume and the LD, APD and TD decreased by 44.8%, 20.9%, 11.8% and 20.0% respectively. The uterine cavity thickness was reduced by

23%, and the length of the cavity was reduced by 27.2% on D7. Uterine involution was correlated inversely with parity when the day of the postpartum period was not taken into account (p= 0.01). However, when the uterine involution was correlated to parity separately, with D1, D2 or D3, no correlations were found. A significant difference occurred at D2, when it was found that the uterus had a smaller volume following cesarean section compared with vaginal delivery (p= 0.04). The high birth weight and breastfeeding were significantly related to uterine involution (p ≤ 0.01 and p= 0.04). Conclusion The sonographic evaluation of the uterus in the early puerperium should consider birth weight, breastfeeding and parity, as well as the delivery route on D2, to identify abnormalities related to uterine involution.
AU - Kristoschek, Juliana Hocevar
AU - Moreira de Sá, Renato Augusto
AU - da Silva, Fernanda Campos
AU - Vellarde, Guillermo Coca
DO - 10.1055/s-0037-1601418
IS - 4
KW - Postpartum period
KW - Ultrasonography
KW - Uterus
PB - Federacao Brasileira das Sociedades de Ginecologia e Obstetricia
PY - 2017
SP - 149
EP - 154
TI - Ultrasonographic Evaluation of Uterine
Involution in the Early Puerperium
T2 - Revista Brasileira de Ginecologia e Obstetricia
VL - 39
ER -
TY - JOUR
AB - Objective: To demonstrate sequential changes of the postpartum uterus using two- and three-dimensional (2D and 3D) ultrasounds and Doppler studies.Methods: Eighty-one women who delivered a singleton at term were recruited for this prospective longitudinal study. Manual and ultrasound examinations of the uterus were performed for seven consecutive weeks. Sequential changes in size of the uterus, endometrial thickness and appearances and Doppler indices of the uterine and arcuate arteries were analyzed.Results: Complete follow ups were achieved in 71 women who had an uncomplicated postpartum course. 2D and 3D ultrasound estimations of uterine volume are highly correlated with each other (r > 0.7), but not manual estimations (r < 0.3). Data generated from 497 3D observations demonstrated rapid involution of the uterus in the first two weeks after delivery. Breastfeeding and parity did not affect uterine involution (r < 0.2). Resistance index (RI) of the uterine artery started to elevate at four weeks after delivery (r > 0.7). RI of the arcuate artery was not significantly changed during the study period (r < 0.2). Uterine involution was independent from progressive thinning of the endometrium and elevation of uterine artery RI. (r < 0.1 and 0.2, respectively).Conclusion: Longitudinal sonographic study showed independent physiologic reversals of uterine volume, endometrium and vascular supply in the first seven weeks following vaginal delivery. Standardization of measurement techniques is essential to apply this information for an early detection of postpartum uterine complications.
AU - Wataganara, Tuangsit

AU - Phithakwatchara, Nisarat
AU - Komoltri, Chulaluk
AU - Tantisirin, Pornpen
AU - Pooliam, Julaporn
AU - Titapant, Vitaya
DA - 2015/12//
DO - 10.3109/14767058.2014.983063
IS - 18
KW - Physiology
KW - postpartum
KW - three-dimensional sonography
KW - uterine artery Doppler
KW - uterine involution
PB - Taylor and Francis Ltd.
PY - 2015
SP - 2221
EP - 2227
TI - Functional three-dimensional sonographic study of the postpartum uterus
T2 - Journal of Maternal-Fetal and Neonatal Medicine
VL - 28
ER -
TY - JOUR
AB - Objective: To establish normal ultrasonographic findings for the postpartum uterus after vaginal delivery, and to characterize associated bleeding patterns. Methods: Postpartum women were scanned by transabdominal ultrasound within 48 h after normal vaginal delivery. Uterine length, uterine width, endometrial stripe thickness and endometrial contents were evaluated by a single sonographer. Patients maintained a daily symptom diary for 6 weeks and were interviewed by telephone at 2 weeks. Statistical analysis was performed using χ2, Fisher's exact test, Student's t test and Pearson correlation. Results: Mean endometrial stripe thickness was 1.1 ± 0.6 cm, mean uterine length was 16.1 ± 1.7 cm and mean uterine width was 8.7 ± 1.0 cm. Postpartum bleeding requiring more than four protective pads per day for ≥ 10 days was associated with a thicker endometrial stripe (1.5 ± 0.7 cm vs. 0.9 ± 0.4 cm, p = 0.006). However, no patients experienced postpartum bleeding complications requiring intervention. Of the 40 women evaluated, 16 had echogenic material in the uterine cavity (mean size 12.7 ± 6.9 cm2). The presence of echogenic material was not associated with the amount or duration of bleeding. Conclusions: Frequent postpartum ultrasonographic findings include a thickened endometrial stripe and echogenic material in the uterine cavity. The echogenic material commonly seen in the endometrial cavity of asymptomatic patients was not associated with the development of bleeding complications.
AU - Sokol, E. R.
AU - Casele, H.
AU - Haney, E. I.
DA - 2004/2//
DO - 10.1080/14767050310001650798
IS - 2
KW - Echogenic material
KW - Postpartum bleeding
KW - Postpartum ultrasound

KW - Uterine cavity
KW - Uterus
PY - 2004
SP - 95
EP - 99
TI - Ultrasound examination of the postpartum uterus: What is normal?
T2 - Journal of Maternal-Fetal and Neonatal Medicine
VL - 15
ER -
TY - RPRT
AU - Shalev, J
AU - Royburt, M
AU - Fite, G
AU - Mashiach, R
AU - Schoenfeld, A
AU - Bar, J
AU - Ben-Rafael, Z
AU - Meizner, I
AU - Shalev, Josef
PY - 2002
TI - Sonographic Evaluation of the Puerperal Uterus: Correlation with Manual Examination
UR - www.karger.com
ER -
TY - JOUR
AB - Background: Data for the causes of maternal deaths are needed to inform policies to improve maternal health. We developed and analysed global, regional, and subregional estimates of the causes of maternal death during 2003-09, with a novel method, updating the previous WHO systematic review. Methods: We searched specialised and general bibliographic databases for articles published between between Jan 1, 2003, and Dec 31, 2012, for research data, with no language restrictions, and the WHO mortality database for vital registration data. On the basis of prespecified inclusion criteria, we analysed causes of maternal death from datasets. We aggregated country level estimates to report estimates of causes of death by Millennium Development Goal regions and worldwide, for main and subcauses of death categories with a Bayesian hierarchical model. Findings: We identified 23 eligible studies (published 2003-12). We included 417 datasets from 115 countries comprising 60 799 deaths in the analysis. About 73% (1 771 000 of 2 443 000) of all maternal deaths between 2003 and 2009 were due to direct obstetric causes and deaths due to indirect causes accounted for 27·5% (672 000, 95% UI 19·7-37·5) of all deaths. Haemorrhage accounted for 27·1% (661 000, 19·9-36·2), hypertensive disorders 14·0% (343 000, 11·1-17·4), and sepsis 10·7% (261 000, 5·9-18·6) of maternal deaths. The rest of deaths were due to abortion (7·9% [193 000], 4·7-13·2), embolism (3·2% [78 000], 1·8-5·5), and all other direct causes of death (9·6% [235 000], 6·5-14·3). Regional estimates varied substantially. Interpretation: Between 2003 and 2009, haemorrhage, hypertensive disorders, and sepsis were responsible for more than half of maternal deaths worldwide. More than a quarter of deaths were attributable to indirect causes. These analyses should inform the prioritisation of health policies, programmes, and funding to reduce maternal deaths at regional and global levels. Further efforts are needed to

improve the availability and quality of data related to maternal mortality. Funding: USAID, the US Fund for UNICEF through a grant from the Bill & Melinda Gates Foundation to CHERG, and The UNDP/UNFPA/UNICEF/WHO/The World Bank Special Programme of Research, Development, and Research Training in Human Reproduction (HRP), Department of Reproductive Health and Research. © 2014 World Health Organization.
AU - Say, Lale
AU - Chou, Doris
AU - Gemmill, Alison
AU - Tunçalp, Özge
AU - Moller, Ann Beth
AU - Daniels, Jane
AU - Gülmezoglu, A. Metin
AU - Temmerman, Marleen
AU - Alkema, Leontine
DO - 10.1016/S2214-109X(14)70227-X
IS - 6
PB - Elsevier Ltd
PY - 2014
TI - Global causes of maternal death: A WHO systematic analysis
T2 - The Lancet Global Health
VL - 2
ER -
TY - JOUR
AB - women who attempted VTOL. Women who planned CD or mon-oamniotic gestations were excluded. We generated two multivariable models to assess factors associated with unplanned CD of one or both twins. Model 1 included maternal demographic and clinical characteristics known before labor. Model 2 included factors from Model 1 with the addition of intrapartum data. Factors in the multivariable models were chosen a priori based on clinical experience or if bivariable associations achieved p< 0.1. Receiver operating characteristic curves were generated for both models. RESULTS: Of 2220 women, 52.4% (N¼1164) elected VTOL. Of women who attempted VTOL, 74% (N¼860) delivered both infants vaginally, while 26% (N¼304) had an unplanned CD. In Model 1, advanced maternal age (aOR 2.24), class II obesity (aOR 1.86), nulliparity (aOR 5.63), and prior CD (aOR 3.39) were associated with unplanned CD (Table). These factors remained significant (p< 0.05) after intrapartum characteristics were introduced in Model 2. Though induction of labor (aOR 1.56) was associated with increased odds of unplanned CD, prematurity (aOR 0.60) was associated with reduced odds of unplanned CD (p< 0.05). The areas under the curve for Model 1 and 2 were 0.728 and 0.748, respectively, demonstrating moderate predictive capacity (Figure). CONCLUSION: Among women with twin gestations choosing VTOL, maternal factors known prior to labor, as well as intrapartum factors, are associated with unplanned CD. Further investigation may elucidate how these findings impact provider counseling and patient decision making, as well as suggest interventions to increase the odds of vaginal delivery of both twins. OBJECTIVE: Postpartum hemorrhage is the third leading cause of maternal mortality, so we aim to review trends over the last 38 years. STUDY DESIGN: We performed a retrospective cohort study of all live births and maternal deaths within 42 days of a pregnancy using data from the Centers for Disease Control and Prevention from 1979-2017. Maternal deaths within 42 days of a pregnancy caused by hemorrhage were identified

based on ICD-9 and ICD-10 codes. Maternal mortality ratios (MMR) per 100,000 live births associated with hemorrhage were calculated for each year. We stratified this ethnicity and additionally calculated unadjusted ratio ratios over 4 decades. Controlling for age and race, we also calculated adjusted rate ratios over the same time period. RESULTS: There were 152,268,131 live births and 29,088 overall maternal deaths in the United States during the study period. During this time, 1,890 (6.5%) were attributed to hemorrhage. The overall MMR secondary to hemorrhage decreased from 1.76 per 100,000 live births in 1979 to 1.71 in 2017. For non-hispanic white women the rate was 1.11 and increased to 1.35 per 100,000, while non-hispanic black women were 4 times as likely to die from hemorrhage in 1999 with a rate of 4.58 and only dropping slightly to 3.21 (Figure). The adjusted rate ratios controlling for age and race show that there has been a 35% decrease over the first ten years of the study period (0.65, 95% CI 0.50, 0.86). In the next decade we only see a 6% decrease compared to the reference year (0.94, 95% CI, 0.73, 1.20), then a 35% (0.65, 95% CI 0.50, 0.86)and 37% (0.63, 95% CI 0.49-0.82) decrease over the next two time periods (Table). CONCLUSION: Maternal mortality associated with hemorrhage has remained stagnant in the United States over the last forty years. An initial decline was noted but has now returned to baseline despite medical interventions. This may be attributed to increase in risk factors for postpartum hemorrhage such as obesity and uterine overdistension. Poster Session I ajog.org

AU - Jayakumaran, Jenani S.
AU - Schuster, Meike
AU - Ananth, Cande V.
DA - 2020/1//
DO - 10.1016/j.ajog.2019.11.276
IS - 1
PB - Elsevier BV
PY - 2020
SP - S178
EP - S179
TI - 260: Postpartum Hemorrhage and its risk of Maternal deaths in the US
T2 - American Journal of Obstetrics and Gynecology
VL - 222
ER -
TY - JOUR

AB - Both the maternal and fetal outcomes of pregnancy vary greatly according to a pregnant woman’s community and her condition. The most devastating outcome is the death of a mother. In 2017, there were ≈295,000 maternal deaths globally with dramatic differences in maternal mortality based on geographic region, country, and women’s underlying conditions. Worldwide, the leading cause of maternal death is hemorrhage, comprising 94% of maternal deaths, with most cases occurring in low- or middle-income countries. Whether a hemorrhage originates from inside the uterus (80%-90%), from lacerations or incisions (10%-20%), or from an underlying coagulopathy (<1%), an acute acquired coagulopathy will evolve unless the hemorrhage is controlled. In low- or middle-income countries, the full range of resources to control hemorrhage is not available, but besides the usual obstetric measures, blood availability, hemostatic medication, and hematologic expertise are necessary to save mothers’ lives. Hemostasis and thrombosis experts can address the disparities in obstetric hemorrhage outcomes not only as providers but as

consultants, researchers, and advocates.
AU - James, Andra H.
AU - Federspiel, Jerome J.
AU - Ahmadzia, Homa K.
DA - 2022/1//
DO - 10.1002/rth2.12656
IS - 1
KW - blood availability
KW - coagulopathy
KW - hemorrhage
KW - maternal mortality
KW - pregnancy
PB - John Wiley and Sons Inc
PY - 2022
TI - Disparities in obstetric hemorrhage outcomes
T2 - Research and Practice in Thrombosis and Haemostasis
VL - 6
ER -
TY - GEN
AB - Postpartum hemorrhage (PPH) is the leading cause of death or severe morbidity for the mother after delivery. As a consequence healthcare staff working in the delivery room should be trained to perform a prompt diagnosis and adequate management of PPH. Uneventful outcome is induced correct identification of the underlying cause of hemorrhage. Ultrasound is a promising technique for the prompt diagnosis of PPH etiology. Indeed, it is easily available, with relatively low cost, not using ionizing radiation, and can be used in different settings including the labor room, the operating theater and at the bedside of an affected women. In order to be effective Obstetricians should have an adequate knowledge of postpartum ultrasonography. In this article, we will review the sonographic findings occurring in PPH, in the differential diagnosis of the underlying cause of hemorrhage, that include retained placenta, morbidly adherent placenta, rupture of the uterus uterine, vascular anomalies of the uterine arteries and uterine inversion. We will also provide an algorithm to manage PPH according to the ultrasonographic findings.
AU - Mappa, Ilenia
AU - Patrizi, Lodovico
AU - Maruotti, Giuseppe Maria
AU - Carbone, Luigi
AU - D'Antonio, Francesco
AU - Rizzo, Giuseppe
DA - 2023/2//
DO - 10.1002/jcu.23343
IS - 2
KW - Bakri balloon
KW - color Doppler
KW - postpartum hemorrhage
KW - retained placenta
KW - ultrasound
PB - John Wiley and Sons Inc
PY - 2023
SP - 362

EP - 372
TI - The role of ultrasound in the diagnosis and management of postpartum hemorrhage
T2 - Journal of Clinical Ultrasound
VL - 51
ER -
TY - RPRT
AU - Instituto Nacional de Salud
PY - 2024
TI - Boletín epidemiológico, semana 1
UR - https://www.ins.gov.co/buscador-eventos/BoletinEpidemiologico/2024_Bolet%C3%ADn_epidemiologico_semana_1.pdf
ER -
TY - JOUR
AB - The ability of ultrasound to predict postpartum hemorrhage remains poorly described. The aim of this study was to evaluate whether ultrasound measurement of intrauterine content can predict blood loss and postpartum hemorrhage after vaginal delivery. We used a preliminary prospective monocentric study of 201 women who delivered vaginally after 34 wk of gestation. Measurements were performed 30–45 min after normal vaginal delivery according to strict ultrasonographic criteria. Analysis of the relationship between ultrasound measurements and hemoglobin loss showed a strong linear correlation ($R^2 = 0.59$ and $R^2 = 0.4$ for isthmic and fundal measurements). The maximal value between the fundal and isthmic measurements seems to provide the best accuracy to predict loss of hemoglobin higher than 3 g/dL (area under the curve [AUC] of the receiver operating characteristic curve, 0.9; 95% confidence interval [CI], [0.76–0.97]) and post-partum hemorrhage (AUC, 0.99; 95%CI, [0.984–0.99]). In case of intrauterine content >2 cm (135/201), the risks of loss of hemoglobin higher than 3 g/dL (5/135 vs. 0/66) and post-partum hemorrhage (11/135 vs. 0/66) were increased, all the more if the intrauterine content was >4 cm (4/16 and 11/16, respectively). Considering the maximal measurement, the most optimal cut-off value for clinical practice could be 2.4 cm (sensibility 100%, specificity 57%) and 4.1 cm (sensibility 100%, specificity 97%) for loss of hemoglobin higher than 3 g/dL and post-partum hemorrhage, respectively.
AU - Hcini, Najeh
AU - Mchirgui, Ali
AU - Pomar, Léo
AU - Beneteau, Samuel
AU - Lambert, Véronique
AU - Carles, Gabriel
DA - 2020/11//
DO - 10.1016/j.ultrasmedbio.2020.07.017
IS - 11
KW - Anemia
KW - Postpartum hemorrhage
KW - Ultrasonography
PB - Elsevier Inc.
PY - 2020
SP - 3145
EP - 3153

TI - Early Prediction of Blood Loss and Postpartum Hemorrhage after Vaginal Delivery by Ultrasound Measurement of Intrauterine Content
T2 - Ultrasound in Medicine and Biology
VL - 46
ER -
TY - BOOK
AU - Organización Panamericana de la Salud
PB - Disponible en: https://iris.paho.org/handle/10665.2/49332
PY - 2012
SN - 9789275074404
TI - Plan de acción para acelerar la reducción de la mortalidad materna y la morbilidad materna grave Publicación Científica CLAP/SMR 1593 Organización Mundial de la Salud Organización Panamericana de la Salud
UR - http://new.paho.org/clap
ER -
TY - JOUR
AU - Solari, Aldo
AU - Solari, Caterina
AU - Wash, Alex
AU - Guerrero, Marcos
IS - 6
PY - 2014
SP - 993
EP - 1003
TI - Hemorrradia del posparto. Principales etiologías, su prevención, diagnósitico y tratamiento
T2 - Rev Médica Clínica Las Condes
VL - 25
ER -
TY - RPRT
AU - Instituto Nacional de Salud
PY - 2023
TI - Boletín epidemiológico, Semana epidemiológica 30
UR - www.ins.gov.co/buscador-eventos/Lineamientos/PRO_Morbili-
ER -
TY - GEN
AB - Purpose of reviewPostpartum hemorrhage (PPH) is the leading preventable cause of maternal morbidity and mortality worldwide. Uterine atony is identified as the underlying etiology in up to 80% of PPH. This serves as a contemporary review of the epidemiology, risk factors, pathophysiology, and treatment of uterine atony.Recent findingsRates of postpartum hemorrhage continue to rise worldwide with the largest fraction attributed to uterine atony. A simple 0-10 numerical rating score for uterine tone was recently validated for use during cesarean delivery and may allow for more standardized assessment in clinical and research settings. The optimal prophylactic dose of oxytocin differs depending on the patient population, but less than 5 units and as low as a fraction of one unit is needed for PPH prevention, with an increased requirements within that range for cesarean birth, those on magnesium, and advanced maternal age. Carbetocin is an appropriate alternative to oxytocin. Misoprostol shows limited to no efficacy for uterine atony in recent studies. Several uncontrolled case studies demonstrate novel mechanical

and surgical interventions for treating uterine atony.SummaryThere is a critical, unmet need for contemporary, controlled studies to address the increasing threat of atonic PPH.
AU - Miller, Hayley E.
AU - Ansari, Jessica R.
DA - 2022/4//
DO - 10.1097/GCO.0000000000000776
IS - 2
KW - postpartum hemorrhage
KW - surgical interventions for atony
KW - uterine atony
KW - uterotonic treatment
PB - Lippincott Williams and Wilkins
PY - 2022
SP - 82
EP - 89
TI - Uterine atony
T2 - Current Opinion in Obstetrics and Gynecology
VL - 34
ER -
TY - GEN
AB - OBJECTIVE:To identify and quantify risk factors for atonic postpartum hemorrhage.DATA SOURCES:PubMed, CINAHL, EMBASE, Web of Science, and and ClinicalTrials.gov databases were searched for English language studies with no restrictions on date or location. Studies included randomized trials, prospective or retrospective cohort studies, and case-control studies of pregnant patients who developed atonic postpartum hemorrhage and reported at least one risk factor.METHODS OF STUDY SELECTION:Title, abstract, and full-text screening were performed using the Raayan web application. Of 1,239 records screened, 27 studies were included in this review. Adjusted or unadjusted odds ratios (ORs), relative risks, or rate ratios were recorded or calculated. For each risk factor, a qualitative synthesis of low and moderate risk of bias studies classifies the risk factor as definite, likely, unclear, or not a risk factor. For risk factors with sufficiently homogeneous definitions and reference ranges, a quantitative meta-analysis of low and moderate risk of bias studies was implemented to estimate a combined OR.TABULATION, INTEGRATION, AND RESULTS:Forty-seven potential risk factors for atonic postpartum hemorrhage were identified in this review, of which 15 were judged definite or likely risk factors. The remaining 32 assessed risk factors showed no association with atonic postpartum hemorrhage or had conflicting or unclear evidence.CONCLUSION:A substantial proportion of postpartum hemorrhage occurs in the absence of recognized risk factors. Many risk factors for atonic hemorrhage included in current risk-assessment tools were confirmed, with the greatest risk conferred by prior postpartum hemorrhage of any etiology, placenta previa, placental abruption, uterine rupture, and multiple gestation. Novel risk factors not currently included in risk-assessment tools included hypertension, diabetes, and ethnicity. Obesity and magnesium were not associated with atonic postpartum hemorrhage in this review.SYSTEMATIC REVIEW REGISTRATION:PROSPERO, CRD42020157521.
AU - Ende, Holly B.
AU - Lozada, M. James

AU - Chestnut, David H.
AU - Osmundson, Sarah S.
AU - Walden, Rachel L.
AU - Shotwell, Matthew S.
AU - Bauchat, Jeanette R.
DA - 2021/2//
DO - 10.1097/AOG.0000000000004228
IS - 2
PB - Lippincott Williams and Wilkins
PY - 2021
SP - 305
EP - 323
TI - Risk Factors for Atonic Postpartum Hemorrhage: A Systematic Review and Meta-analysis
T2 - Obstetrics and Gynecology
VL - 137
ER -
TY - JOUR
AU - Bienstock, Jessica L.
AU - Eke, Ahizechukwu C.
AU - Hueppchen, Nancy A.
DA - 2021/4//
DO - 10.1056/NEJMra1513247
ED - Longo, Dan L.
IS - 17
PY - 2021
SP - 1635
EP - 1645
TI - Postpartum Hemorrhage
T2 - New England Journal of Medicine
UR - http://www.nejm.org/doi/10.1056/NEJMra1513247
VL - 384
ER -
TY - GEN
AB - Postpartum hemorrhage is a leading cause of maternal morbidity and mortality, and uterine atony is the leading cause of postpartum hemorrhage. Risk factors for uterine atony include induced or augmented labor, preeclampsia, chorio-amnionitis, obesity, multiple gestation, polyhydramnios, and prolonged second stage of labor. Although a risk assessment is recommended for all parturients, many women with uterine atony do not have risk factors, making uterine atony difficult to predict. Oxytocin is the first-line drug for prevention and treatment of uterine atony. It is a routine component of the active management of the third stage of labor. An oxytocin bolus dose as low as 1 IU is sufficient to produce satisfactory uterine tone in almost all women undergoing elective cesarean delivery. However, a higher bolus dose (3 IU) or infusion rate is recommended for women undergoing intrapartum cesarean delivery. Carbetocin, available in many countries, is a synthetic oxytocin analog with a longer duration than oxytocin that allows bolus administration without an infusion. Second line uterotonic agents include ergot alkaloids (ergometrine and methylergonovine) and the prostaglandins, carboprost and misoprostol. These drugs work by a different mechanism to oxytocin and should be

administered early for uterine atony refractory to oxytocin. Rigorous studies are lacking, but methylergonovine and carboprost are likely superior to misoprostol. Currently, the choice of second-line agent should be based on their adverse effect profile and patient comorbidities. Surgical and radiologic management of uterine atony includes uterine tamponade using balloon catheters and compression sutures, and percutaneous transcatheter arterial embolization.
AU - Balki, M.
AU - Wong, C. A.
DA - 2021/11//
DO - 10.1016/j.ijoa.2021.103207
KW - Carboprost
KW - Ergot alkaloids
KW - Misoprostol
KW - Oxytocin
KW - Uterine atony
PB - Churchill Livingstone
PY - 2021
TI - Refractory uterine atony: still a problem after all these years
T2 - International Journal of Obstetric Anesthesia
VL - 48
ER -
TY - JOUR
AB - BACKGROUND: Postpartum hemorrhage is a leading source of maternal morbidity and mortality worldwide with uterine atony identified as the underlying cause in up to 80% of cases. Several measures have been utilized to report uterine tone. The most commonly reported measure is a 0 to 10 numeric rating scale, but this scale has not been tested for reliability or agreement between different raters. OBJECTIVE: The primary purpose of this study was to evaluate the interrater reliability and agreement of the 0 to 10 visual numeric rating scale of uterine tone during cesarean delivery. A secondary purpose was to obtain estimates of scale responsiveness and minimal clinically important difference. STUDY DESIGN: Between August and November of 2018, obstetricians used a 0 to 10 numeric rating score to independently rate uterine tone at 3 and 10 minutes after cesarean delivery by palpation of the uterus. Of note, “0” represented “no tone” and “10” represented excellent tone. Each obstetrician independently and blinded to the other's score pointed to a numeric rating scale held by the anesthesiologist through a clear sterile drape. Intraclass correlation coefficients and Bland-Altman analysis were used to assess interrater reliability and agreement, respectively. Standardized response mean and standard error of measurement were used to obtain estimates of responsiveness and minimal clinically important difference, respectively. RESULTS: A total of 82 and 84 pairs of scores were collected at 3 and 10 minutes, respectively, from pairs of 62 unique obstetricians. The mean±standard deviation difference in scores between rater 1 and rater 2 was 0.4±1.4 at 3 minutes and 0.1±1.1 at 10 minutes. Intraclass correlation coefficients for a future single rater (intraclass correlation coefficient [1, 1]) at 3 and 10 minutes were 0.67 (95% confidence interval, 0.53–0.77) and 0.61 (95% confidence interval, 0.46–0.73), and for the average between 2 future raters (intraclass correlation coefficient [1, 2]), they were 0.80 (95% confidence interval, 0.71–0.87) and 0.76 (95% confidence interval, 0.63–0.84), indicating good and excellent reliability, respectively. Bland-Altman analysis estimated 95% limit of agreement between raters of −2.4 (95%

confidence interval, −3.0 to −1.9) to 3.1 (95% confidence interval, 2.6–3.7) at 3 minutes and −2.1 (95% confidence interval, −2.5 to −1.7) to 2.4 (95% confidence interval, 2.0–2.8) at 10 minutes, consistent with good interrater agreement at both time points. The standardized response mean from 3 to 10 minutes after delivery was 1.1 (n=81). Standard error of measurement was 1.0 (95% confidence interval, 0.9–1.1) at 3 minutes and 0.8 (95% confidence interval, 0.7–0.9) at 10 minutes. CONCLUSION: The 0 to 10 numeric rating scale for uterine tone demonstrated good to excellent interrater reliability with 1 and 2 raters, respectively, and good interrater agreement. The scale was responsive to within-parturient change in tone, and preliminary estimates of the minimal clinically important difference were obtained. The 0 to 10 numeric rating scale for uterine tone may be a reliable, standardized tool for future research in reporting degree of uterotonic contraction during cesarean delivery.
AU - Cole, Naida M.
AU - Abushoshah, Ibrahim
AU - Fields, Kara G.
AU - Carusi, Daniela A.
AU - Robinson, Julian N.
AU - Bateman, Brian T.
AU - Farber, Michaela K.
DA - 2021/5//
DO - 10.1016/j.ajogmf.2021.100342
IS - 3
KW - numeric rating scale
KW - uterine atony
KW - uterine tone
KW - uterotonic
PB - Elsevier Inc.
PY - 2021
TI - The interrater reliability and agreement of a 0 to 10 uterine tone score in cesarean delivery
T2 - American Journal of Obstetrics and Gynecology MFM
VL - 3
ER -
TY - JOUR
AU - De Winter, J
AU - De Raedemaecker, H
AU - Muys, J
AU - Jacquemyn, Y.
PY - 2017
SP - 207
EP - 216
TI - The value of postpartum ultrasound for the diagnosis of retained products of conception: A systematic review
T2 - Facts Views Vis Obgyn
VL - 19
ER -
TY - JOUR
AB - Background: Although maternal deaths are rare in developed regions, the morbidity associated with severe postpartum hemorrhage (SPPH) remains a major

problem. To determine the prevalence and risk factors of SPPH, we analyzed data of women who gave birth in Guangzhou Medical Centre for Critical Pregnant Women, which received a large quantity of critically ill obstetric patients who were transferred from other hospitals in Southern China. Methods: In this study, we conducted a retrospective case-control study to determine the prevalence and risk factors for SPPH among a cohort of women who gave birth after 28 weeks of gestation between January 2015 and August 2019. SPPH was defined as an estimated blood loss ≥1000 mL and total blood transfusion≥4 units. Logistic regression analysis was used to identify independent risk factors for SPPH. Results: SPPH was observed in 532 mothers (1.56%) among the total population of 34,178 mothers. Placenta-related problems (55.83%) were the major identified causes of SPPH, while uterine atony without associated retention of placental tissues accounted for 38.91%. The risk factors for SPPH were maternal age < 18 years (adjusted OR [aOR] = 11.52, 95% CI: 1.51–87.62), previous cesarean section (aOR = 2.57, 95% CI: 1.90–3.47), history of postpartum hemorrhage (aOR = 4.94, 95% CI: 2.63–9.29), conception through in vitro fertilization (aOR = 1.78, 95% CI: 1.31–2.43), pre-delivery anemia (aOR = 2.37, 95% CI: 1.88–3.00), stillbirth (aOR = 2.61, 95% CI: 1.02–6.69), prolonged labor (aOR = 5.24, 95% CI: 3.10–8.86), placenta previa (aOR = 9.75, 95% CI: 7.45–12.75), placenta abruption (aOR = 3.85, 95% CI: 1.91–7.76), placenta accrete spectrum (aOR = 8.00, 95% CI: 6.20–10.33), and macrosomia (aOR = 2.30, 95% CI: 1.38–3.83). Conclusion: Maternal age < 18 years, previous cesarean section, history of PPH, conception through IVF, pre-delivery anemia, stillbirth, prolonged labor, placenta previa, placental abruption, PAS, and macrosomia were risk factors for SPPH. Extra vigilance during the antenatal and peripartum periods is needed to identify women who have risk factors and enable early intervention to prevent SPPH.

AU - Liu, Chen ning
AU - Yu, Fu bing
AU - Xu, Yun zhe
AU - Li, Jin sheng
AU - Guan, Zhi hong
AU - Sun, Man na
AU - Liu, Chen an
AU - He, Fang
AU - Chen, Dun jin
DA - 2021/12//
DO - 10.1186/s12884-021-03818-1
IS - 1
KW - Causes
KW - Postpartum hemorrhage
KW - Risk factors
PB - BioMed Central Ltd
PY - 2021
TI - Prevalence and risk factors of severe postpartum hemorrhage: a retrospective cohort study
T2 - BMC Pregnancy and Childbirth
VL - 21
ER -
TY - GEN
AB - OBJECTIVE:To identify and quantify risk factors for atonic postpartum hemorrhage.DATA SOURCES:PubMed, CINAHL, EMBASE, Web of Science, and and

ClinicalTrials.gov databases were searched for English language studies with no restrictions on date or location. Studies included randomized trials, prospective or retrospective cohort studies, and case-control studies of pregnant patients who developed atonic postpartum hemorrhage and reported at least one risk factor.METHODS OF STUDY SELECTION:Title, abstract, and full-text screening were performed using the Raayan web application. Of 1,239 records screened, 27 studies were included in this review. Adjusted or unadjusted odds ratios (ORs), relative risks, or rate ratios were recorded or calculated. For each risk factor, a qualitative synthesis of low and moderate risk of bias studies classifies the risk factor as definite, likely, unclear, or not a risk factor. For risk factors with sufficiently homogeneous definitions and reference ranges, a quantitative meta-analysis of low and moderate risk of bias studies was implemented to estimate a combined OR.TABULATION, INTEGRATION, AND RESULTS:Forty-seven potential risk factors for atonic postpartum hemorrhage were identified in this review, of which 15 were judged definite or likely risk factors. The remaining 32 assessed risk factors showed no association with atonic postpartum hemorrhage or had conflicting or unclear evidence.CONCLUSION:A substantial proportion of postpartum hemorrhage occurs in the absence of recognized risk factors. Many risk factors for atonic hemorrhage included in current risk-assessment tools were confirmed, with the greatest risk conferred by prior postpartum hemorrhage of any etiology, placenta previa, placental abruption, uterine rupture, and multiple gestation. Novel risk factors not currently included in risk-assessment tools included hypertension, diabetes, and ethnicity. Obesity and magnesium were not associated with atonic postpartum hemorrhage in this review.SYSTEMATIC REVIEW REGISTRATION:PROSPERO, CRD42020157521.

AU - Ende, Holly B.
AU - Lozada, M. James
AU - Chestnut, David H.
AU - Osmundson, Sarah S.
AU - Walden, Rachel L.
AU - Shotwell, Matthew S.
AU - Bauchat, Jeanette R.
DA - 2021/2//
DO - 10.1097/AOG.0000000000004228
IS - 2
PB - Lippincott Williams and Wilkins
PY - 2021
SP - 305
EP - 323
TI - Risk Factors for Atonic Postpartum Hemorrhage: A Systematic Review and Meta-analysis
T2 - Obstetrics and Gynecology
VL - 137
ER -
TY - JOUR
AU - Bienstock, Jessica L.
AU - Eke, Ahizechukwu C.
AU - Hueppchen, Nancy A.
DA - 2021/4//
DO - 10.1056/NEJMra1513247

ED - Longo, Dan L.
IS - 17
PY - 2021
SP - 1635
EP - 1645
TI - Postpartum Hemorrhage
T2 - New England Journal of Medicine
UR - http://www.nejm.org/doi/10.1056/NEJMra1513247
VL - 384
ER -
TY - JOUR
AB - Objectives This study aims to use the high-quality national monitoring data from the China's National Maternal Near Miss Surveillance System (NMNMSS) to ascertain the incidence, trends and risk factors of obstetric massive blood transfusion (MBT) from 2012 to 2019 in China and determine its clinical outcomes. Settings Observational study of hospitalised pregnancies who had given birth or ended their pregnancy among member hospitals of NMNMSS. Participants 11 667 406 women were included in this study. Primary and secondary outcome measures We screened for the incidence, trends, risk factors and main reasons for obstetric MBT, and the outcomes after obstetric MBT. MBT was defined as the transfusion of ≥5 units of red blood cells or ≥1000 mL of whole blood. The incidence of MBT was defined as the MBT cases per 10 000 pregnancies. Results Obstetric MBT occurred in 27 626 cases, corresponding to an incidence of 23.68 per 10 000 maternities, which exhibited an increasing trend in China during 2012-2019 (14.03-29.59 per 10 000 maternities, p for trend <0.001). Obstetric MBT was mainly associated with amniotic fluid embolism, uterine atony, abnormal placenta, severe anaemia, ectopic pregnancy, abortion, caesarean section, advanced maternal age and multiparous from biological effect. While from sociological effects, uterine atony, severe anaemia and placenta previa are the top three complications which more likely to undergo obstetric MBT in the Chinese population. Overall, the secular trends of hysterectomy incidence (25.07%-9.92%) and MMR during hospitalisation (21.41‰-7.48‰) among women who underwent MBT showed decreasing trends (p for trend <0.001). Conclusion To minimise the incidence of obstetric MBT, more attention should be paid to education on the importance of the antenatal visit, evidence-based transfusion practice and females who are multiparous and have an advanced age, amniotic fluid embolism, uterine atony, severe anaemia and placenta previa.
AU - Xie, Yanxia
AU - Liang, Juan
AU - Mu, Yi
AU - Liu, Zheng
AU - Wang, Yanping
AU - Dai, Li
AU - Li, Xiaohong
AU - Li, Qi
AU - Li, Mingrong
AU - Chen, Peiran
AU - Zhu, Jun
AU - Wang, Xiaodong
DA - 2021/9//
DO - 10.1136/bmjopen-2020-047983

IS - 9
KW - fetal medicine
KW - maternal medicine
KW - public health
PB - BMJ Publishing Group
PY - 2021
TI - Incidence, trends and risk factors for obstetric massive blood transfusion in China from 2012 to 2019: An observational study
T2 - BMJ Open
VL - 11
ER -
TY - JOUR
AB - This study aims to evaluate the feasibility and clinical interest of shear wave elastography, by quantitatively estimating the baseline stiffness of the myometrium before and after placental expulsion. We conducted a prospective cohort study of women at term, without known risk factors for postpartum hemorrhage, who gave birth via spontaneous labor in our tertiary center. Myometrium tonicity was evaluated based on measurements of shear wave speed (SWS) in the anterior uterine corpus. All data points were collected by a single operator. Measurements were carried out at three different time points: after fetal delivery (T1), after placental delivery (T2) and 30 min after placental delivery (T3). Our primary objective was to assess the feasibility of this new imaging technique. Ten valid SWS measurements obtained at each of the three different time points were considered as a positive primary outcome. Our secondary objectives were to evaluate the difference in median myometrial shear wave velocity between each time point, as well as to determine the correlation between myometrial shear wave velocity and patients' characteristics. 38 women were recruited during the study period, of whom 34 met the study criteria. 1017 SWS measurements were obtained. The median time to perform measurements was 16 s for one value, and 2 min 56 s for ten. For 11 women (32%) it was not possible to achieve ten SWS at T1 as placental expulsion immediately followed the birth of the newborn. One patient experienced placental retention and only measurements at T1 were performed. For all other patients, we were successfully able to obtain all measures as intended. There was no difference in the mean shear wave speed between the three time points. After adjustments for confounders, we observed a significant correlation for total blood loss (correlation coefficient = − 0.26, $p < 0.001$, units of oxytocin (correlation coefficient = − 0.34, $p = 0.03$), and newborn weight (correlation coefficient = − 0.08, $p = 0.001$). It is feasible to assess uterine tonicity by shear wave imaging, after placental expulsion. We did not observe a variance in uterine tonicity between the three time points. Women who had higher blood loss, received more units of oxytocin and/or those with newborns of a higher weight exhibited lower shear wave speed measures.
AU - Sichitiu, Joanna
AU - Meuwly, Jean Yves
AU - Baud, David
AU - Desseauve, David
DA - 2021/12//
DO - 10.1038/s41598-021-89756-6
IS - 1
PB - Nature Research

PY - 2021
TI - Using shear wave elastography to assess uterine tonicity after vaginal delivery
T2 - Scientific Reports
VL - 11
ER -
TY - JOUR
AB - Objectives Sonoelastography is an ultrasound-imaging technique that measures tissue strain. The aim of this study was to define, in a systematic manner, specific sonoelastographic characteristics of the myometrium, fibroids and adenomyosis, to evaluate the feasibility of sonoelastography in patients with suspected gynecological pathology and to compare the results with histology and/or magnetic resonance imaging (MRI)-based diagnoses. Methods We performed a prospective observational cohort study between 2009 and 2011. Two-hundred and eighteen women with suspected gynecological pathology underwent routine transvaginal ultrasound and additional real-time sonographic elastography. Sixty-nine of the 218 women underwent MRI and/or histological examination and were included in the final analysis. Acquisition of elastographic images was standardized. We analyzed the elastographic characteristics of myometrium, fibroids and adenomyosis. An independent observer, unaware of clinical, histological or MRI findings, evaluated the recorded elastographic images and cineloops. These elastographic-based diagnoses were compared with histology and/or MRI diagnoses. Results With elastography, the uterus was well delineated from the surrounding bowel. The myometrium was uniform in color in 49% of the cases, with a main color of purple or dark blue, indicating stiffer tissue. Fibroids and adenomyosis had different elastographic characteristics and different color patterns. In general, fibroids were darker and adenomyosis was brighter than adjacent myometrium. The agreement between elastography-based diagnosis of fibroids and adenomyosis with MRI-based diagnosis was excellent; with histology-based diagnosis, agreement was substantial for fibroids and adenomyosis. Conclusions Elastography is able to identify clear discriminating characteristics of the uterus, fibroids and adenomyosis, and elastography-based diagnoses are in excellent agreement with those of MRI. Agreement between elastography-based diagnosis of adenomyosis and histology is substantial but not optimal.
AU - Stoelinga, B.
AU - Hehenkamp, W. J.K.
AU - Brölmann, H. A.M.
AU - Huirne, J. A.F.
DA - 2014/2//
DO - 10.1002/uog.12519
IS - 2
KW - adenomyosis
KW - elastography
KW - fibroids
KW - ultrasound
PY - 2014
SP - 218
EP - 226
TI - Real-time elastography for assessment of uterine disorders

T2 - Ultrasound in Obstetrics and Gynecology
VL - 43
ER -
TY - JOUR
AB - Neurobehavior represents development of the central nervous system (CNS). Fetuses and newborns exhibit a large number of endogenously generated motor patterns, among which general movements are often investigated pre- and post-natally. Spontaneous activity is probably a more sensitive indicator of brain dysfunction than reactivity to sensory stimuli while testing reflexes. Nutritional stress at critical times during fetal development can have persistent and potentially irreversible effects particularly on brain growth and function. Unfavorable intrauterine environment can affect adversely brain growth. All endogenously generated movement patterns from un-stimulated CNS might be observed as early as from the seven to eight weeks' gestation, with a rich repertoire of movements within the next two or three weeks, continuing for five to six months postnatally. It is still uncertain whether a new scoring system for prenatal neurological assessment will be adequate for the distinction between normal and abnormal fetuses in low-risk pregnancies. The continuity of behavioral patterns from prenatal to postnatal life might answer these intriguing questions. © 2011 by Walter de Gruyter Berlin New York.
AU - Stanojevic, Milan
AU - Kurjak, Asim
AU - Salihagić-Kadić, Aida
AU - Vasilj, Oliver
AU - Miskovic, Berivoj
AU - Shaddad, Afaf Naim
AU - Ahmed, Badreldeen
AU - Tomasović, Sanja
DA - 2011/3//
DO - 10.1515/JPM.2011.004
IS - 2
KW - Development of central nervous system
KW - fetal neurobehavior
KW - four-dimensional ultrasound
KW - general movements
KW - neonatal neurobehavior
PY - 2011
SP - 171
EP - 177
TI - Neurobehavioral continuity from fetus to neonate
T2 - Journal of Perinatal Medicine
VL - 39
ER -
TY - RPRT
AU - Lucas, A
AU - Makrides, M
AU - Ziegler, E E
PY - 2010
SP - 137
EP - 151

TI - Importance of Growth for Health and Development
T2 - Nestlé Nutr Inst Workshop Ser Pediatr Program
VL - 65
ER -
TY - JOUR
AB - Early human brain development constitutes a sequence of intricate processes resulting in the ontogeny of functionally operative neural circuits. Developmental trajectories of early brain network formation are genetically programmed and can be modified by epigenetic and environmental influences. Such alterations may exert profound effects on neurodevelopment, potentially persisting throughout the lifespan. This review focuses on the critical period of fetal and early postnatal brain development. Here we collate findings from neuroimaging studies, with a particular focus on functional MRI research that interrogated early brain network development in both health and high-risk or disease states. First, we will provide an overview of the developmental processes that take place from the embryonic period through early infancy in order to contextualize brain network formation. Second, functional brain network development in the typically developing brain will be discussed. Third, we will touch on prenatal and perinatal risk factors that may interfere with the trajectories of functional brain wiring, including prenatal substance exposure, maternal mental illness and preterm birth. Collectively, studies have revealed the blueprint of adult human brain organization to be present in the neonatal brain. Distinct attributes of human brain architecture have even been detected in the developing fetal brain from as early as 24 postconceptional weeks. During postnatal brain development, the brain's wiring pattern is further sculpted and modulated to become the full facsimile of the adult human brain, with functional brain network refinement being more rigorous than structural brain network maturation. Advances in neuroimaging techniques have paved the way towards a comprehensive understanding of the maturational pathways of brain network development and of how early developmental adversity may affect these trajectories. Such insights are fundamental for our understanding of human brain functioning, for early identification of infants at risk, as well as for future neuroprotective strategies.
AU - Keunen, Kristin
AU - Counsell, Serena J.
AU - Benders, Manon J.N.L.
DA - 2017/10//
DO - 10.1016/j.neuroimage.2017.01.047
KW - Brain networks
KW - Connectivity
KW - Fetal
KW - Functional MRI
KW - Neonatal
PB - Academic Press Inc.
PY - 2017
SP - 2
EP - 14
TI - The emergence of functional architecture during early brain development
T2 - NeuroImage
VL - 160
ER -

TY - GEN
AB - The prenatal and neonatal periods are two of the most important developmental stages of the human brain. It is therefore crucial to understand normal brain development and how early connections are established during these periods, in order to advance the state of knowledge on altered brain development and eventually identify early brain markers of neurodevelopmental disorders and diseases. In this systematic review (Prospero ID: CRD42024511365), we compiled resting state functional magnetic resonance imaging (fMRI) studies in healthy fetuses and neonates, in order to outline the main characteristics of typical development of the functional brain connectivity during the prenatal and neonatal periods. A systematic search of five databases identified a total of 12 573 articles. Of those, 28 articles met pre-established selection criteria based determined by the authors after surveying and compiling the major limitations reported within the literature. Inclusion criteria were: (1) resting state studies; (2) presentation of original results; (3) use of fMRI with minimum one Tesla; (4) a population ranging from 20 weeks of GA to term birth (around 37–42 weeks of PMA); (5) singleton pregnancy with normal development (absence of any complications known to alter brain development). Exclusion criteria were: (1) preterm studies; (2) post-mortem studies; (3) clinical or pathological studies; (4) twin studies; (5) papers with a sole focus on methodology (i.e. focused on tool and analysis development); (6) volumetric studies; (7) activation map studies; (8) cortical analysis studies; (9) conference papers. A risk of bias assessment was also done to evaluate each article's methodological rigor. 1877 participants were included across all the reviewed articles. Results consistently revealed a developmental gradient of increasing functional brain connectivity from posterior to anterior regions and from proximal-to-distal regions. A decrease in local small-world organization shortly after birth was also observed; small-world characteristics were present in fetuses and newborns, but appeared weaker in the latter group. Also, the posterior-to-anterior gradient could be associated with earlier development of the sensorimotor networks in the posterior regions while more complex higher-order networks (e.g. attention-related) mature later in the anterior regions. The main limitations of this systematic review stem from the inherent limitations of functional imaging in fetuses, mainly: unevenly distributed populations and limited sample sizes; fetal movements in the womb and other imaging obstacles; and a large voxel resolution when imaging a small brain. Another limitation specific to this review is the relatively small number of included articles compared to very a large search result, which may have led to relevant articles having been overlooked.
AU - Desrosiers, Jérémi
AU - Caron-Desrochers, Laura
AU - René, Andréanne
AU - Gaudet, Isabelle
AU - Pincivy, Alix
AU - Paquette, Natacha
AU - Gallagher, Anne
DA - 2024/8//
DO - 10.1016/j.neubiorev.2024.105778
KW - Antenatal
KW - Brain development
KW - Brain imaging
KW - FMRI

KW - Fetal
KW - Functional connectivity
KW - Neonatal
KW - Neural networks
KW - Prenatal
KW - Systematic review
KW - Typical development
PB - Elsevier Ltd
PY - 2024
TI - Functional connectivity development in the prenatal and neonatal stages measured by functional magnetic resonance imaging: A systematic review
T2 - Neuroscience and Biobehavioral Reviews
VL - 163
ER -
TY - GEN
AB - Unique from other fetal anatomical systems, the central nervous system (CNS) starts development early in the embryonic period shortly after fertilization before most patients are even aware they are pregnant. Maturation throughout pregnancy involve complicated structural and functional changes, most likely below the resolution of testing to detect. During this time, the fetal CNS is susceptible to lesions that reflect trimester-specific adverse events. Neonatal neurological status with childhood sequelae can result from combinations of antenatal, peripartum and neonatal adverse events. Person-specific clinical management choices must consider the timing of multiple mechanisms that can alter neurodevelopment including genetic causes, aetiologies after conception as well as communicable and non-communicable conditions that result in anomalous or destructive brain lesions. The appearance of the fetal brain also changes significantly through gestation as different structures mature and the cerebral cortex in particular increases in size and complexity. Therefore, obstetrical imagers and maternal fetal medicine physicians need to be aware of the expected evolving appearances of the healthy fetal brain as the fetus advances in gestation. Often when fetal CNS pathology is detected or anticipated during pregnancy, there is understandably significant parental anxiety regarding the long-term implications of their child's neurodevelopmental prognosis. In these instances, Maternal Fetal Medicine specialists often collaborate with Pediatric Neurologists in the antenatal period regarding diagnoses that anticipate neonatal or later childhood neurologic sequelae. Potential adverse outcomes are discussed with prospective parents to be integrated into choices based on shared decisions.
AU - Soliman, Nancy
AU - Kuret, Verena
AU - Chan, Elaine
AU - Smith, Christopher
AU - Thomas, Mary Anne
AU - Mahallati, Houman
AU - Grosjean, Heidi
AU - Friebe, Erika
AU - Rusnell, Leah
DA - 2024/11//
DO - 10.1016/j.siny.2024.101555
KW - Fetal neuroimaging

KW - Interdisciplinary fetal neurology consultations
KW - Maternal-fetal medicine surveillance
KW - Parental counselling
PB - W.B. Saunders Ltd
PY - 2024
TI - Overview of reproductive and pregnancy health principles and practice used by maternal-fetal medicine specialists for fetal-neonatal neurology consultants
T2 - Seminars in Fetal and Neonatal Medicine
ER -
TY - GEN
AB - Fetal brain development is a complex process involving different stages of growth and organization which are crucial for the development of brain circuits and neural connections. Fetal atlases and labeled datasets are promising tools to investigate prenatal brain development. They support the identification of atypical brain patterns, providing insights into potential early signs of clinical conditions. In a nutshell, prenatal brain imaging and post-processing via modern tools are a cutting-edge field that will significantly contribute to the advancement of our understanding of fetal development. In this work, we first provide terminological clarification for specific terms (i.e., “brain template” and “brain atlas”), highlighting potentially misleading interpretations related to inconsistent use of terms in the literature. We discuss the major structures and neurodevelopmental milestones characterizing fetal brain ontogenesis. Our main contribution is the systematic review of 18 prenatal brain atlases and 3 datasets. We also tangentially focus on clinical, research, and ethical implications of prenatal neuroimaging.
AU - Ciceri, Tommaso
AU - Casartelli, Luca
AU - Montano, Florian
AU - Conte, Stefania
AU - Squarcina, Letizia
AU - Bertoldo, Alessandra
AU - Agarwal, Nivedita
AU - Brambilla, Paolo
AU - Peruzzo, Denis
DA - 2024/4//
DO - 10.1016/j.neuroimage.2024.120603
KW - Brain atlas
KW - Brain dataset
KW - Fetus
KW - Magnetic resonance imaging
PB - Academic Press Inc.
PY - 2024
TI - Fetal brain MRI atlases and datasets: A review
T2 - NeuroImage
VL - 292
ER -
TY - GEN
AB - The human brain develops slowly and over a long period of time which lasts for almost three decades. This enables good spatio-temporal resolution of histogenetic and neurogenetic events as well as an appropriate and clinically

relevant timing of these events. In order to successfully apply in vivo neuroimaging data, in analyzing both the normal brain development and the neurodevelopmental origin of major neurological and mental disorders, it is important to correlate these neuroimaging data with the existing data on morphogenetic, histogenetic and neurogenetic events. Furthermore, when performing such correlation, the genetic, genomic, and molecular biology data on phenotypic specification of developing brain regions, areas and neurons should also be included. In this review, we focus on early developmental periods (form 8 postconceptional weeks to the second postnatal year) and describe the microstructural organization and neural circuitry elements of the fetal and early postnatal human cerebrum.
AU - Kostović, I.
AU - Sedmak, G.
AU - Judaš, M.
DA - 2019/3//
DO - 10.1016/j.neuroimage.2018.12.043
KW - Cerebral cortex
KW - Human brain development
KW - Subplate
KW - Telencephalon
PB - Academic Press Inc.
PY - 2019
SP - 743
EP - 773
TI - Neural histology and neurogenesis of the human fetal and infant brain
T2 - NeuroImage
VL - 188
ER -
TY - GEN
AB - Background: Preterm birth is a serious and common pregnancy complication. The burden is particularly high in low- and middle-income countries where available care is often inadequate to ensure preterm newborn survival. Administration of antenatal corticosteroids (ACS) is recommended as the standard care for the management of women at risk of imminent preterm birth but its coverage varies globally. Efforts to improve preterm newborn survival have largely been focused on optimising the coverage of ACS use. However, the benefits and harms of such strategies are unclear. Objectives: To determine the relative benefits and risks of individual patient protocols, health service policies, educational interventions or other strategies which aim to optimise the use of ACS for anticipated preterm birth. Search methods: We searched Cochrane Pregnancy and Childbirth’s Trials Register, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) (26 September 2019), and reference lists of retrieved studies. Selection criteria: We planned to include randomised controlled trials (RCTs), randomised at individual or cluster level, and quasi-randomised trials that assessed strategies to optimise (either by increasing or restricting) the administration of ACS compared with usual care amongst women at risk of preterm birth. Our primary outcomes were perinatal death and a composite outcome of offspring mortality and early or late neurodevelopmental morbidity. Data collection and analysis: Two review authors independently assessed studies for inclusion. All three review authors independently extracted data and assessed risk of bias. We

used narrative synthesis to analyse results, as we were unable to pool data from the included studies. We assessed the certainty of evidence using the GRADE approach. Main results: We included three cluster-RCTs, all assessing the effects of a multifaceted strategy aiming to promote the use of ACS among women at risk of preterm birth. We did not identify any trials assessing strategies to restrict the use of ACS versus usual care. Two of the included trials assessed use of ACS in high-resource hospital settings. The third trial, the Antenatal Corticosteroid Trial (ACT) was a multi-site trial conducted in rural and semi-urban settings of six low- and middle-income countries in South Asia, sub-Saharan Africa and Central and South America. In two trials, promoting the use of ACS resulted in increased use of ACS, whereas one trial did not find a difference in the rate of ACS administration compared to usual care. Whilst we included three studies, we were unable to pool the data in meta-analysis due to outcomes not being reported across all studies, or outcome results being reported in different ways. The main source of data in this review is from the ACT trial. We assessed the ACT trial as high risk for performance and selective reporting bias. In the protocol for this review, we planned to report all settings and subgroup by low-middle versus high-income countries; these planned analyses were not possible in this version of the review, although adding further studies in future updates may allow us to carry out planned subgroup analyses. The ACT trial was conducted in low-resource settings and reported data on appropriate ACS treatment and inappropriate ACS treatment. Although a strategy of promoting the administration of ACS compared to routine care may increase appropriate ACS treatment (RR 4.34, 95%CI 3.59 to 5.25; 1 study; n = 4389; low-certainty evidence), it may also increase inappropriate ACS treatment (RR 9.11 95%CI 8.04 to 10.33, 1 study, n = 89,237; low-certainty evidence). In low-resource settings, a strategy of promoting the administration of ACS probably increases population level perinatal death by 3 per 1000 infants (risk ratio (RR) 1.11, 95% confidence interval (CI) 1.04 to 1.19; 1 study; n = 100,705; moderate-certainty evidence); stillbirth by 2 per 1000 infants (RR 1.11, 95% CI 1.02 to 1.21; 1 study; n = 100,705; moderate-certainty evidence); and neonatal death before 28 days by 2 per 1000 infants (RR 1.12, 95% CI 1.02 to 1.23; 1 study; n = 100,705; moderate-certainty evidence); may increase the risk for 'suspected' maternal infection or inflammation (RR 1.49, 95% CI 1.32 to 1.68; 1 study; n = 99,742; low-certainty evidence); and make little or no difference to the risk of maternal mortality (RR 1.11, 95% CI 0.64 to 1.92; 1 study; n = 99,742; low-certainty evidence) compared to routine care. Included trials did not report on the composite outcomes offspring mortality, early neurodevelopmental morbidity or late neurodevelopmental morbidity; and offspring mortality or severe neonatal morbidity. Authors' conclusions: In low-resource settings, a strategy of actively promoting the use of ACS in women at risk of preterm birth may increase ACS use in the target population, but may also carry a substantial risk of unnecessary exposure of ACS to women in whom ACS is not indicated. At the population level, these effects are probably associated with increased risks of stillbirth, perinatal death, neonatal death before 28 days, and maternal infection. The findings of this review support a more conservative approach to clinical protocols and clinical decision-making particularly in low-resource settings, along the lines of the World Health Organization's ACS 2015 recommendations, which take into account both the established clinical efficacy of ACS when used in the correct situation and context, and the possibility of important adverse effects when certain conditions are not met. Given the unanticipated results of the ACT trial, further research on

strategies to optimise the use of ACS in low-resource settings is justified.
AU - Rohwer, Anke C.
AU - Oladapo, Olufemi T.
AU - Hofmeyr, G. Justus
DA - 2020/5//
DO - 10.1002/14651858.CD013633
IS - 5
PB - John Wiley and Sons Ltd
PY - 2020
TI - Strategies for optimising antenatal corticosteroid administration for women with anticipated preterm birth
T2 - Cochrane Database of Systematic Reviews
VL - 2020
ER -
TY - JOUR
AB - Importance: The Antenatal Late Preterm Steroids (ALPS) trial changed clinical practice in the United States by finding that antenatal betamethasone at 34 to 36 weeks decreased short-term neonatal respiratory morbidity. However, the trial also found increased risk of neonatal hypoglycemia after betamethasone. This follow-up study focused on long-term neurodevelopmental outcomes after late preterm steroids. Objective: To evaluate whether administration of late preterm (34-36 completed weeks) corticosteroids affected childhood neurodevelopmental outcomes. Design, Setting, and Participants: Prospective follow-up study of children aged 6 years or older whose birthing parent had enrolled in the multicenter randomized clinical trial, conducted at 13 centers that participated in the Maternal-Fetal Medicine Units (MFMU) Network cycle from 2011-2016. Follow-up was from 2017-2022. Exposure: Twelve milligrams of intramuscular betamethasone administered twice 24 hours apart. Main Outcome and Measures: The primary outcome of this follow-up study was a General Conceptual Ability score less than 85 (-1 SD) on the Differential Ability Scales, 2nd Edition (DAS-II). Secondary outcomes included the Gross Motor Function Classification System level and Social Responsiveness Scale and Child Behavior Checklist scores. Multivariable analyses adjusted for prespecified variables known to be associated with the primary outcome. Sensitivity analyses used inverse probability weighting and also modeled the outcome for those lost to follow-up. Results: Of 2831 children, 1026 enrolled and 949 (479 betamethasone, 470 placebo) completed the DAS-II at a median age of 7 years (IQR, 6.6-7.6 years). Maternal, neonatal, and childhood characteristics were similar between groups except that neonatal hypoglycemia was more common in the betamethasone group. There were no differences in the primary outcome, a general conceptual ability score less than 85, which occurred in 82 (17.1%) of the betamethasone vs 87 (18.5%) of the placebo group (adjusted relative risk, 0.94; 95% CI, 0.73-1.22). No differences in secondary outcomes were observed. Sensitivity analyses using inverse probability weighting or assigning outcomes to children lost to follow-up also found no differences between groups. Conclusion and Relevance: In this follow-up study of a randomized clinical trial, administration of antenatal corticosteroids to persons at risk of late preterm delivery, originally shown to improve short-term neonatal respiratory outcomes but with an increased rate of hypoglycemia, was not associated with adverse childhood neurodevelopmental outcomes at age 6 years or older..
AU - Gyamfi-Bannerman, Cynthia
AU - Clifton, Rebecca G.

AU - Tita, Alan T.N.
AU - Blackwell, Sean C.
AU - Longo, Monica
AU - De Voest, Jessica A.
AU - O'Shea, T. Michael
AU - Bousleiman, Sabine Z.
AU - Ortiz, Felecia
AU - Rouse, Dwight J.
AU - Metz, Torri D.
AU - Saade, George R.
AU - Rood, Kara M.
AU - Heyborne, Kent D.
AU - Thorp, John M.
AU - Swamy, Geeta K.
AU - Grobman, William A.
AU - Gibson, Kelly S.
AU - El-Sayed, Yasser Y.
AU - Macones, George A.
DA - 2024/5//
DO - 10.1001/jama.2024.4303
IS - 19
PB - American Medical Association
PY - 2024
SP - 1629
EP - 1637
TI - Neurodevelopmental Outcomes after Late Preterm Antenatal Corticosteroids: The ALPS Follow-Up Study
T2 - JAMA
VL - 331
ER -
TY - JOUR
AB - OBJECTIVE: To systematically review the proportions of infants with early exposure to antenatal corticosteroids but born at term or late preterm, and short term and long term outcomes. DESIGN: Systematic review and meta-analyses. DATA SOURCES: Eight databases searched from 1 January 2000 to 1 February 2023, reflecting recent perinatal care, and references of screened articles. ELIGIBILITY CRITERIA FOR SELECTING STUDIES: Randomised controlled trials and population based cohort studies with data on infants with early exposure to antenatal corticosteroids (<34 weeks) but born at term (≥37 weeks), late preterm (34-36 weeks), or term/late preterm combined. DATA EXTRACTION AND SYNTHESIS: Two reviewers independently screened titles, abstracts, and full text articles and assessed risk of bias (Cochrane risk of bias tool for randomised controlled trials and Newcastle-Ottawa scale for population based studies). Reviewers extracted data on populations, exposure to antenatal corticosteroids, and outcomes. The authors analysed randomised and cohort data separately, using random effects meta-analyses. MAIN OUTCOME MEASURES: The primary outcome was the proportion of infants with early exposure to antenatal corticosteroids but born at term. Secondary outcomes included the proportions of infants born late preterm or term/late preterm combined after early exposure to antenatal corticosteroids and short term and long term outcomes versus non-exposure for the three gestational time points (term, late preterm,

term/late preterm combined). RESULTS: Of 14 799 records, the reviewers screened 8815 non-duplicate titles and abstracts and assessed 713 full text articles. Seven randomised controlled trials and 10 population based cohort studies (1.6 million infants total) were included. In randomised controlled trials and population based data, ~40% of infants with early exposure to antenatal corticosteroids were born at term (low or very low certainty). Among children born at term, early exposure to antenatal corticosteroids versus no exposure was associated with increased risks of admission to neonatal intensive care (adjusted odds ratio 1.49, 95% confidence interval 1.19 to 1.86, one study, 5330 infants, very low certainty; unadjusted relative risk 1.69, 95% confidence interval 1.51 to 1.89, three studies, 1 176 022 infants, I2=58%, τ2=0.01, low certainty), intubation (unadjusted relative risk 2.59, 1.39 to 4.81, absolute effect 7 more per 1000, 95% confidence interval from 2 more to 16 more, one study, 8076 infants, very low certainty, one study, 8076 infants, very low certainty), reduced head circumference (adjusted mean difference -0.21, 95% confidence interval -0.29 to -0.13, one study, 183 325 infants, low certainty), and any long term neurodevelopmental or behavioural disorder in population based studies (eg, any neurodevelopmental or behavioural disorder in children born at term, adjusted hazard ratio 1.47, 95% confidence interval 1.36 to 1.60, one study, 641 487 children, low certainty). CONCLUSIONS: About 40% of infants exposed to early antenatal corticosteroids were born at term, with associated adverse short term and long term outcomes (low or very low certainty), highlighting the need for caution when considering antenatal corticosteroids. SYSTEMATIC REVIEW REGISTRATION: PROSPERO CRD42022360079.
AU - Ninan, Kiran
AU - Gojic, Anja
AU - Wang, Yanchen
AU - Asztalos, Elizabeth V.
AU - Beltempo, Marc
AU - Murphy, Kellie E.
AU - McDonald, Sarah D.
DA - 2023/8//
DO - 10.1136/bmj-2023-076035
PB - NLM (Medline)
PY - 2023
SP - e076035
EP - e076035
TI - The proportions of term or late preterm births after exposure to early antenatal corticosteroids, and outcomes: systematic review and meta-analysis of 1.6 million infants
T2 - BMJ (Clinical research ed.)
VL - 382
ER -
TY - RPRT
AU - Reddy, Uma M
AU - Deshmukh, Uma
AU - Dude, Annie
AU - Harper, Lorie
AU - Osmundson, Sarah S
TI - Society for Maternal-Fetal Medicine Consult Series #58: Use of antenatal corticosteroids for individuals at risk for late preterm delivery Society for

Maternal-Fetal Medicine (SMFM)
ER -
TY - JOUR
AB - Antenatal steroid therapy is increasingly central to the obstetrical management of women at imminent risk of preterm birth. For women likely to deliver between 24 and 34 weeks' gestation, antenatal steroid therapy is the standard of care, conferring sizable benefits and few risks in high-resource environments when appropriately targeted. Recent studies have focused on antenatal steroid use in periviable and late preterm populations, and in term cesarean deliveries. As a result, antenatal steroid therapy has now been applied from 22 to 39+6 weeks of estimated gestational age. There is also an increased appreciation that the vast majority of randomized control data informing the use of antenatal steroids are derived from predominantly high-resource, White populations. Accordingly, a sizable amount of work has recently been undertaken to test how to safely use antenatal steroids in low- and middle-resource environments, wherein the often high rates of preterm birth make these low-cost, easily administered interventions an attractive proposition. It is likely underappreciated by the obstetrical and neonatal communities that the overall efficacy of antenatal steroid therapy is highly variable (including when preterm risk is accurately assessed), the treatment regimens used are largely arbitrary, dosing is suprapharmacologic for effect, and the benefit–risk balance is significantly and differentially modified by gestation. It is also very likely that the patients consenting to receive these treatments are similarly unaware of the complex balance of potential benefits and harms. Although a small number of follow-up studies present a generally benign picture of long-term antenatal steroid risk, several large, population-based retrospective studies have identified associations between antenatal steroid use, childhood mental disease, and newborn infections that warrant urgent attention. Of particular contemporary importance are emergent efforts to optimize antenatal steroid regimens on the basis of the pharmacokinetics and pharmacodynamics of the agents themselves, the need for better targeting of these potent drugs, and clear articulation of the potential benefits and harms of antenatal steroid use at differing stages of pregnancy and in different delivery contexts.
AU - Jobe, Alan H.
AU - Goldenberg, Robert L.
AU - Kemp, Matthew W.
DA - 2024/3//
DO - 10.1016/j.ajog.2023.09.013
IS - 3
KW - betamethasone
KW - clinical
KW - dosing
KW - outcomes
KW - prematurity
KW - trials
PB - Elsevier Inc.
PY - 2024
SP - 330
EP - 339
TI - Antenatal corticosteroids: an updated assessment of anticipated benefits and potential risks

T2 - American Journal of Obstetrics and Gynecology
VL - 230
ER -
TY - JOUR
AB - Objective To evaluate the effectiveness of antenatal corticosteroids given at ≥34 weeks' gestation. Design Systematic review with meta-analysis. Data sources Electronic databases were searched from their inception to February 2016. Eligibility criteria for study selection Randomized clinical trials comparing antenatal corticosteroids with placebo or no treatment in women with a singleton pregnancy at ≥34 weeks' gestation. Trials on antenatal steroids in women expected to deliver late preterm (340-366 weeks) and trials given before planned cesarean delivery at term (≥37 weeks) were included. Data synthesis The primary outcome was the incidence of severe respiratory distress syndrome (RDS). The summary measures were reported as relative risks or mean differences with 95% confidence intervals. Results Six trials, including 5698 singleton pregnancies, were analyzed. Three included 3200 women at 340-366 weeks' gestation and at risk of imminent premature delivery at the time of hospital admission. The three other trials included 2498 women undergoing planned cesarean delivery at ≥37 weeks. Overall, infants of mothers who received antenatal corticosteroids at ≥34 weeks had a significantly lower risk of RDS (relative risk 0.74, 95% confidence interval 0.61 to 0.91), mild RDS (0.67, 0.46 to 0.96), moderate RDS (0.39, 0.18 to 0.89), transient tachypnea of the newborn (0.56, 0.37 to 0.86), severe RDS (0.55, 0.33 to 0.91), use of surfactant, and mechanical ventilation, and a significantly lower time receiving oxygen (mean difference-2.06 hours, 95% confidence interval-2.17 to-1.95), lower maximum inspired oxygen concentration (-0.66%,-0.69% to-0.63%), shorter stay on a neonatal intensive care unit (-7.64 days,-7.65 to-7.64), and higher APGAR scores compared with controls. Infants of mothers who received antenatal betamethasone at 340-366 weeks' gestation had a significantly lower incidence of transient tachypnea of the newborn (relative risk 0.72, 95% confidence interval 0.56 to 0.92), severe RDS (0.60, 0.33 to 0.94), and use of surfactant (0.61, 0.38 to 0.99). Infants of mothers undergoing planned cesarean delivery at ≥37 weeks' gestation who received prophylactic antenatal corticosteroids 48 hours before delivery had a significantly lower risk of RDS (0.40, 0.27 to 0.59), mild RDS (0.43, 0.26 to 0.72), moderate RDS (0.40, 0.18 to 0.88), transient tachypnea of the newborn (0.38, 0.25 to 0.57), and mechanical ventilation (0.19, 0.08 to 0.43), and significantly less time receiving oxygen (mean difference-2.06 hours, 95% confidence interval-2.17 to-1.95), lower percentage of maximum inspired oxygen concentration (-0.66%,-0.69% to-0.63%), shorter stay in neonatal intensive care (-7.44 days,-7.44 to-7.43), and a higher APGAR score at one and at five minutes. Conclusions Antenatal steroids at ≥34 weeks' gestation reduce neonatal respiratory morbidity. A single course of corticosteroids can be considered for women at risk of imminent late premature delivery 340-366 weeks' gestation, as well as for women undergoing planned cesarean delivery at ≥37 weeks' gestation.
AU - Saccone, Gabriele
AU - Berghella, Vincenzo
DO - 10.1136/bmj.i5044
PB - BMJ Publishing Group
PY - 2016
TI - Antenatal corticosteroids for maturity of term or near term fetuses: Systematic review and meta-analysis of randomized controlled trials

T2 - BMJ (Online)
VL - 355
ER -
TY - GEN
AB - Importance: Animal studies have found that antenatal corticosteroids affect many organs across multiple stages of life. However, the long-term outcomes in human children are not well understood. Objective: To conduct a systematic review and meta-analysis of long-term outcomes associated with preterm exposure to antenatal corticosteroids compared with no exposure in all children as well as children with preterm and full-term birth. Data Sources: Academic databases were searched for articles published from January 1, 2000, to October 29, 2021, including Ovid MEDLINE, Ovid Embase, PsycInfo, CINAHL (Cumulative Index of Nursing and Allied Health Literature), Web of Science, ClinicalTrials.gov, and Google Scholar. References of articles were also searched for relevant studies. Study Selection: Randomized clinical trials (RCTs), quasi-RCTs, and cohort studies that assessed long-term neurodevelopmental, psychological, or other outcomes at 1 year or older in those who had preterm exposure to antenatal corticosteroids were included. No language restrictions were set. Data Extraction and Synthesis: Two reviewers independently extracted data using a piloted data extraction form. Data on study population, pregnancy characteristics, exposure to antenatal corticosteroids, and outcomes were collected. Preferred Reporting Items for Systematic Reviews and Meta-analyses reporting guidelines were followed, and random-effects models were used for the meta-analysis. Main Outcomes and Measures: The primary outcome was an author-defined composite of any adverse neurodevelopmental and/or psychological disorder. The secondary outcomes included specific measures of psychological disorders; neurodevelopmental delay; and anthropometric, metabolic, and cardiorespiratory outcomes. Results: A total of 30 studies met the inclusion criteria, and involved more than 1.25 million children who were at least 1 year of age when the outcomes were assessed. Exposure to a single course of antenatal corticosteroids for children with extremely preterm birth was associated with a significant reduction in risk of neurodevelopmental impairment (adjusted odds ratio, 0.69 [95% CI, 0.57-0.84]; I2= 0%; low certainty). For children with late-preterm birth, exposure to antenatal corticosteroids was associated with a higher risk of investigation for neurocognitive disorders (n = 25668 children; adjusted hazard ratio [aHR], 1.12 [95% CI, 1.05-1.20]; low certainty). For children with full-term birth, exposure to antenatal corticosteroids was associated with a higher risk of mental or behavioral disorders (n = 641 487 children; aHR, 1.47 [95% CI, 1.36-1.60]; low certainty) as well as proven or suspected neurocognitive disorders (n = 529205 children; aHR, 1.16 [95% CI, 1.10-1.21]; low certainty). Conclusions and Relevance: Results of this study showed that exposure to a single course of antenatal corticosteroids was associated with a significantly lower risk of neurodevelopmental impairment in children with extremely preterm birth but a significantly higher risk of adverse neurocognitive and/or psychological outcomes in children with late-preterm and full-term birth, who made up approximately half of those with exposure to antenatal corticosteroids. The findings suggest a need for caution in administering antenatal corticosteroids.
AU - Ninan, Kiran
AU - Liyanage, Sugee K.
AU - Murphy, Kellie E.
AU - Asztalos, Elizabeth V.

AU - McDonald, Sarah D.
DA - 2022/6//
DO - 10.1001/jamapediatrics.2022.0483
IS - 6
PB - American Medical Association
PY - 2022
SP - e220483
EP - e220483
TI - Evaluation of Long-term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids: A Systematic Review and Meta-analysis
T2 - JAMA Pediatrics
VL - 176
ER -
TY - GEN
AB - Background Administration of antenatal corticosteroids (ANC) for impending preterm delivery beyond 34 weeks of gestation continues to be a controversial issue despite various guidelines for obstetricians and gynaecologists. Objective To compare outcomes following exposure to ANC for infants born between 34-36+6 weeks' gestation. Methods A systematic review of randomised controlled trials (RCT) reporting neonatal outcomes after ANC exposure between 34-36+6 weeks' gestation using Cochrane methodology. Databases including PubMed, Embase, Emcare, Cochrane Central library and Google Scholar were searched in May 2020. Primary outcomes: (1) Need for respiratory support (Mechanical ventilation, CPAP, high flow) or oxygen (2) Hypoglycemia. Secondary outcomes included respiratory distress syndrome (RDS), transient tachypnoea of newborn (TTN), need for neonatal resuscitation at birth [only in the delivery room immediately after birth (not in neonatal intensive care unit (NICU)], admission to NICU, mortality and developmental follow up. Level of evidence (LOE) was summarised by GRADE guidelines. Main results Seven RCTs (N = 4144) with low to high risk of bias were included. Only one RCT was from high income countries, Meta-analysis (random-effects model) showed (1) reduced need for respiratory support [5 RCTs (N = 3844); RR = 0.68 (0.47-0.98), p = 0.04; I2 = 55%; LOE: Moderate] and (2) higher risk of neonatal hypoglycaemia [4 RCTs (N = 3604); RR = 1.61 (1.38-1.87), p<0.00001; I2 = 0%; LOE: High] after ANC exposure. Neonates exposed to ANC had reduced need for resuscitation at birth. The incidence of RDS, TTN and surfactant therapy did not differ significantly. None of the included studies reported long-term developmental follow up. Conclusions Moderate quality evidence indicates that ANC exposure reduced need for respiratory support, and increased the risk of hypoglycaemia in late preterm neonates. Large definitive trials with adequate follow up for neurodevelopmental outcomes are required to assess benefits and risks of ANC in this population.
AU - Deshmukh, Mangesh
AU - Patole, Sanjay
DA - 2021/3//
DO - 10.1371/journal.pone.0248774
IS - 3 March
PB - Public Library of Science
PY - 2021
TI - Antenatal corticosteroids for impending late preterm (34-36+6 weeks) deliveries-A systematic review and meta-analysis of RCTs
T2 - PLoS ONE

VL - 16
ER -
TY - GEN
AB - Background: Despite the widespread use of antenatal corticosteroids to prevent respiratory distress syndrome (RDS) in preterm infants, there is currently no consensus as to the type of corticosteroid to use, dose, frequency, timing of use or the route of administration. Objectives: To assess the effects on fetal and neonatal morbidity and mortality, on maternal morbidity and mortality, and on the child and adult in later life, of administering different types of corticosteroids (dexamethasone or betamethasone), or different corticosteroid dose regimens, including timing, frequency and mode of administration. Search methods: For this update, we searched Cochrane Pregnancy and Childbirth Group's Trials Register, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) (9 May 2022) and reference lists of retrieved studies. Selection criteria: We included all identified published and unpublished randomised controlled trials or quasi-randomised controlled trials comparing any two corticosteroids (dexamethasone or betamethasone or any other corticosteroid that can cross the placenta), comparing different dose regimens (including frequency and timing of administration) in women at risk of preterm birth. We planned to exclude cross-over trials and cluster-randomised trials. We planned to include studies published as abstracts only along with studies published as full-text manuscripts. Data collection and analysis: At least two review authors independently assessed study eligibility, extracted data and assessed the risk of bias of included studies. Data were checked for accuracy. We assessed the certainty of the evidence using GRADE. Main results: We included 11 trials (2494 women and 2762 infants) in this update, all of which recruited women who were at increased risk of preterm birth or had a medical indication for preterm birth. All trials were conducted in high-income countries. Dexamethasone versus betamethasone. Nine trials (2096 women and 2319 infants) compared dexamethasone versus betamethasone. All trials administered both drugs intramuscularly, and the total dose in the course was consistent (22.8 mg or 24 mg), but the regimen varied. We assessed one new study to have no serious risk of bias concerns for most outcomes, but other studies were at moderate (six trials) or high (two trials) risk of bias due to selection, detection and attrition bias. Our GRADE assessments ranged between high- and low-certainty, with downgrades due to risk of bias and imprecision. Maternal outcomes. The only maternal primary outcome reported was chorioamnionitis (death and puerperal sepsis were not reported). Although the rate of chorioamnionitis was lower with dexamethasone, we did not find conclusive evidence of a difference between the two drugs (risk ratio (RR) 0.71, 95% confidence interval (CI) 0.48 to 1.06; 1 trial, 1346 women; moderate-certainty evidence). The proportion of women experiencing maternal adverse effects of therapy was lower with dexamethasone; however, there was not conclusive evidence of a difference between interventions (RR 0.63, 95% CI 0.35 to 1.13; 2 trials, 1705 women; moderate-certainty evidence). Infant outcomes. We are unsure whether the choice of drug makes a difference to the risk of any known death after randomisation, because the 95% CI was compatible with both appreciable benefit and harm with dexamethasone (RR 1.03, 95% CI 0.66 to 1.63; 5 trials, 2105 infants; moderate-certainty evidence). The choice of drug may make little or no difference to the risk of RDS (RR 1.06, 95% CI 0.91 to 1.22; 5 trials, 2105 infants; high-certainty evidence). While there may be little or no difference in the risk of intraventricular haemorrhage (IVH), there was substantial unexplained

statistical heterogeneity in this result (average (a) RR 0.71, 95% CI 0.28 to 1.81; 4 trials, 1902 infants; I^2 = 62%; low-certainty evidence). We found no evidence of a difference between the two drugs for chronic lung disease (RR 0.92, 95% CI 0.64 to 1.34; 1 trial, 1509 infants; moderate-certainty evidence), and we are unsure of the effects on necrotising enterocolitis, because there were few events in the studies reporting this outcome (RR 5.08, 95% CI 0.25 to 105.15; 2 studies, 441 infants; low-certainty evidence). Longer-term child outcomes. Only one trial consistently followed up children longer term, reporting at two years' adjusted age. There is probably little or no difference between dexamethasone and betamethasone in the risk of neurodevelopmental disability at follow-up (RR 1.02, 95% CI 0.85 to 1.22; 2 trials, 1151 infants; moderate-certainty evidence). It is unclear whether the choice of drug makes a difference to the risk of visual impairment (RR 0.33, 95% CI 0.01 to 8.15; 1 trial, 1227 children; low-certainty evidence). There may be little or no difference between the drugs for hearing impairment (RR 1.16, 95% CI 0.63 to 2.16; 1 trial, 1227 children; moderate-certainty evidence), motor developmental delay (RR 0.89, 95% CI 0.66 to 1.20; 1 trial, 1166 children; moderate-certainty evidence) or intellectual impairment (RR 0.97, 95% CI 0.79 to 1.20; 1 trial, 1161 children; moderate-certainty evidence). However, the effect estimate for cerebral palsy is compatible with both an important increase in risk with dexamethasone, and no difference between interventions (RR 2.50, 95% CI 0.97 to 6.39; 1 trial, 1223 children; low-certainty evidence). No trials followed the children beyond early childhood. Comparisons of different preparations and regimens of corticosteroids. We found three studies that included a comparison of a different regimen or preparation of either dexamethasone or betamethasone (oral dexamethasone 32 mg versus intramuscular dexamethasone 24 mg; betamethasone acetate plus phosphate versus betamethasone phosphate; 12-hourly betamethasone versus 24-hourly betamethasone). The certainty of the evidence for the main outcomes from all three studies was very low, due to small sample size and risk of bias. Therefore, we were limited in our ability to draw conclusions from any of these studies. Authors' conclusions: Overall, it remains unclear whether there are important differences between dexamethasone and betamethasone, or between one regimen and another. Most trials compared dexamethasone versus betamethasone. While for most infant and early childhood outcomes there may be no difference between these drugs, for several important outcomes for the mother, infant and child the evidence was inconclusive and did not rule out significant benefits or harms. The evidence on different antenatal corticosteroid regimens was sparse, and does not support the use of one particular corticosteroid regimen over another.

AU - Williams, Myfanwy J.
AU - Ramson, Jenny A.
AU - Brownfoot, Fiona C.
DA - 2022/8//
DO - 10.1002/14651858.CD006764.pub4
IS - 8
PB - John Wiley and Sons Ltd
PY - 2022
TI - Different corticosteroids and regimens for accelerating fetal lung maturation for babies at risk of preterm birth
T2 - Cochrane Database of Systematic Reviews
VL - 2022

ER -
TY - CONF
AB - Background: Late preterm birth is associated with short-term respiratory and adaptive problems. Although antenatal corticosteroids seem to reduce the respiratory burden, this may come at the cost of adverse neuropsychological outcomes later in life. This impact has not been investigated. Objective: Herein, we investigate what the short- and long-term neurodevelopmental effects of a single course of betamethasone in simulated late preterm birth. Study Design: Time-mated pregnant does received 0.1 mg/kg betamethasone (n=8) or 1 mL saline intramuscular (n=6) at the postconceptional ages of 28 and 29 days. The antenatal corticosteroid dose and scheme were based on previous studies and were comparable with routine clinical use. Cesarean delivery was done on postconceptional age 30 days (term=31 days), and new-born rabbits were foster-cared for 28 days and were thereafter cared for in group housing. Neonatal lung function testing and short-term neurobehavioral testing was done. Open field, spontaneous alternation, and novel object recognition tests were subsequently performed at 4 and 8 weeks of age. On postnatal day 1 and at 8 weeks, a subgroup was euthanized and transcardially perfuse fixated. Ex vivo high-resolution Magnetic Resonance Imaging was used to calculate the Diffusion Tensor Imaging-derived fractional anisotropy and mean diffusivity. Fixated brains underwent processing and were serial sectioned, and a set of 3 coronal sections underwent anti-NeuN, Ki67, and terminal deoxynucleotidyl transferase dUTP nick end labeling staining. Results: Antenatal corticosteroid exposure was associated with improved neonatal lung function, yet resulted in a long-term growth deficit that coincided with a persistent neurobehavioral deficit. We demonstrated lower neonatal motor scores; a persistent anxious behavior in the open field test with more displacements, running, and self-grooming episodes; persistent lower alternation scores in the T-Maze test; and lower discriminatory indexes in the novel object recognition. On neuropathological assessment, antenatal corticosteroid exposure was observed to result in a persistent lower neuron density and fewer Ki67+ cells, particularly in the hippocampus and the corpus callosum. This coincided with lower diffusion tensor imaging-derived fractional anisotropy scores in the same key regions. Conclusion: Clinical equivalent antenatal corticosteroid exposure in this late preterm rabbit model resulted in improved neonatal lung function. However, it compromised neonatal and long-term neurocognition.
AU - van der Merwe, Johannes
AU - van der Veeken, Lennart
AU - Inversetti, Annalisa
AU - Galgano, Angela
AU - Valenzuela, Ignacio
AU - Salaets, Thomas
AU - Ferraris, Sebastiano
AU - Vercauteren, Tom
AU - Toelen, Jaan
AU - Deprest, Jan
DA - 2022/6//
DO - 10.1016/j.ajog.2021.11.1370
IS - 6
KW - antenatal corticosteroid
KW - betamethasone
KW - late preterm

KW - neurobehavior
KW - neurocognition
PB - Elsevier Inc.
PY - 2022
SP - 850.e1
EP - 850.e21
TI - Neurocognitive sequelae of antenatal corticosteroids in a late preterm rabbit model
T2 - American Journal of Obstetrics and Gynecology
VL - 226
ER -
TY - GEN
AB - Background: Infants born preterm (before 37 weeks' gestation) are at risk of respiratory distress syndrome (RDS) and need for respiratory support due to lung immaturity. One course of prenatal corticosteroids, administered to women at risk of preterm birth, reduces the risk of respiratory morbidity and improves survival of their infants, but these benefits do not extend beyond seven days. Repeat doses of prenatal corticosteroids have been used for women at ongoing risk of preterm birth more than seven days after their first course of corticosteroids, with improvements in respiratory outcomes, but uncertainty remains about any long-term benefits and harms. This is an update of a review last published in 2015. Objectives: To assess the effectiveness and safety, using the best available evidence, of a repeat dose(s) of prenatal corticosteroids, given to women who remain at risk of preterm birth seven or more days after an initial course of prenatal corticosteroids with the primary aim of reducing fetal and neonatal mortality and morbidity. Search methods: For this update, we searched Cochrane Pregnancy and Childbirth's Trials Register, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP), and reference lists of retrieved studies. Selection criteria: Randomised controlled trials, including cluster-randomised trials, of women who had already received one course of corticosteroids seven or more days previously and were still at risk of preterm birth, randomised to further dose(s) or no repeat doses, with or without placebo. Quasi-randomised trials were excluded. Abstracts were accepted if they met specific criteria. All trials had to meet criteria for trustworthiness, including a search of the Retraction Watch database for retractions or expressions of concern about the trials or their publications. Data collection and analysis: We used standard Cochrane Pregnancy and Childbirth methods. Two review authors independently selected trials, extracted data, and assessed trial quality and scientific integrity. We chose primary outcomes based on clinical importance as measures of effectiveness and safety, including serious outcomes, for the women and their fetuses/infants, infants in early childhood (age two to less than five years), the infant in mid- to late childhood (age five to less than 18 years) and the infant as an adult. We assessed risk of bias at the outcome level using the RoB 2 tool and assessed certainty of evidence using GRADE. Main results: We included 11 trials (4895 women and 5975 babies). High-certainty evidence from these trials indicated that treatment of women who remain at risk of preterm birth seven or more days after an initial course of prenatal corticosteroids with repeat dose(s) of corticosteroids, compared with no repeat corticosteroid treatment, reduced the risk of their infants experiencing the primary infant outcome of RDS (risk ratio (RR) 0.82, 95% confidence interval (CI) 0.74 to 0.90; 3540 babies; number needed to

treat for an additional beneficial outcome (NNTB) 16, 95% CI 11 to 29) and had little or no effect on chronic lung disease (RR 1.00, 95% CI 0.83 to 1.22; 5661 babies). Moderate-certainty evidence indicated that the composite of serious infant outcomes was probably reduced with repeat dose(s) of corticosteroids (RR 0.88, 95% CI 0.80 to 0.97; 9 trials, 5736 babies; NNTB 39, 95% CI 24 to 158), as was severe lung disease (RR 0.83, 95% CI 0.72 to 0.97; NNTB 45, 95% CI 27 to 256; 4955 babies). Moderate-certainty evidence could not exclude benefit or harm for fetal or neonatal or infant death less than one year of age (RR 0.95, 95% CI 0.73 to 1.24; 5849 babies), severe intraventricular haemorrhage (RR 1.13, 95% CI 0.69 to 1.86; 5066 babies) and necrotising enterocolitis (RR 0.84, 95% CI 0.59 to 1.22; 5736 babies). In women, moderate-certainty evidence found little or no effect on the likelihood of a caesarean birth (RR 1.03, 95% CI 0.98 to 1.09; 4266 mothers). Benefit or harm could not be excluded for maternal death (RR 0.32, 95% 0.01 to 7.81; 437 women) and maternal sepsis (RR 1.13, 95% CI 0.93 to 1.39; 4666 mothers). The evidence was unclear for risk of adverse effects and discontinuation of therapy due to maternal adverse effects. No trials reported breastfeeding status at hospital discharge or risk of admission to the intensive care unit. At early childhood follow-up, moderate- to high-certainty evidence identified little or no effect of exposure to repeat prenatal corticosteroids compared with no repeat corticosteroids for primary outcomes relating to neurodevelopment (neurodevelopmental impairment: RR 0.97, 95% CI 0.85 to 1.10; 3616 children), survival without neurodevelopmental impairment (RR 1.01, 95% CI 0.98 to 1.04; 3845 children) and survival without major neurodevelopmental impairment (RR 1.02, 95% CI 0.98 to 1.05; 1816 children). An increase or decrease in the risk of death since randomisation could not be excluded (RR 1.06, 95% CI 0.81 to 1.40; 5 trials, 4565 babies randomised). At mid-childhood follow-up, moderate-certainty evidence identified little or no effect of exposure to repeat prenatal corticosteroids compared with no repeat corticosteroids on survival free of neurocognitive impairment (RR 1.01, 95% CI 0.95 to 1.08; 963 children) or survival free of major neurocognitive impairment (RR 1.00, 95% CI 0.97 to 1.04; 2682 children). Benefit or harm could not be excluded for death since randomisation (RR 0.93, 95% CI 0.69 to 1.26; 2874 babies randomised) and any neurocognitive impairment (RR 0.96, 95% CI 0.72 to 1.29; 897 children). No trials reported data for follow-up into adolescence or adulthood. Risk of bias across outcomes was generally low although there were some concerns of bias. For childhood follow-up, most outcomes had some concerns of risk of bias due to missing data from loss to follow-up. Authors' conclusions: The short-term benefits for babies included less respiratory distress and fewer serious health problems in the first few weeks after birth with repeat dose(s) of prenatal corticosteroids for women still at risk of preterm birth seven days or more after an initial course. The current available evidence reassuringly shows no significant harm for the women or child in early and mid-childhood, although no benefit. Further research is needed on the long-term benefits and risks for the baby into adulthood.
AU - Walters, Anthony
AU - McKinlay, Christopher
AU - Middleton, Philippa
AU - Harding, Jane E.
AU - Crowther, Caroline A.
DA - 2022/4//
DO - 10.1002/14651858.CD003935.pub5

IS - 4
PB - John Wiley and Sons Ltd
PY - 2022
TI - Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes
T2 - Cochrane Database of Systematic Reviews
VL - 2022
ER -
TY - GEN
AB - Background: Respiratory morbidity including respiratory distress syndrome (RDS) is a serious complication of preterm birth and the primary cause of early neonatal mortality and disability. Despite early evidence indicating a beneficial effect of antenatal corticosteroids on fetal lung maturation and widespread recommendations to use this treatment in women at risk of preterm delivery, some uncertainty remains about their effectiveness particularly with regard to their use in lower-resource settings, different gestational ages and high-risk obstetric groups such as women with hypertension or multiple pregnancies. This updated review (which supersedes an earlier review Crowley 1996) was first published in 2006 and subsequently updated in 2017. Objectives: To assess the effects of administering a course of corticosteroids to women prior to anticipated preterm birth (before 37 weeks of pregnancy) on fetal and neonatal morbidity and mortality, maternal mortality and morbidity, and on the child in later life. Search methods: We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (3 September 2020), ClinicalTrials.gov, the databases that contribute to the WHO International Clinical Trials Registry Platform (ICTRP) (3 September 2020), and reference lists of the retrieved studies. Selection criteria: We considered all randomised controlled comparisons of antenatal corticosteroid administration with placebo, or with no treatment, given to women with a singleton or multiple pregnancy, prior to anticipated preterm delivery (elective, or following rupture of membranes or spontaneous labour), regardless of other co-morbidity, for inclusion in this review. Data collection and analysis: We used standard Cochrane Pregnancy and Childbirth methods for data collection and analysis. Two review authors independently assessed trials for inclusion, assessed risk of bias, evaluated trustworthiness based on predefined criteria developed by Cochrane Pregnancy and Childbirth, extracted data and checked them for accuracy, and assessed the certainty of the evidence using the GRADE approach. Primary outcomes included perinatal death, neonatal death, RDS, intraventricular haemorrhage (IVH), birthweight, developmental delay in childhood and maternal death. Main results: We included 27 studies (11,272 randomised women and 11,925 neonates) from 20 countries. Ten trials (4422 randomised women) took place in lower- or middle-resource settings. We removed six trials from the analysis that were included in the previous version of the review; this review only includes trials that meet our pre-defined trustworthiness criteria. In 19 trials the women received a single course of steroids. In the remaining eight trials repeated courses may have been prescribed. Fifteen trials were judged to be at low risk of bias, two had a high risk of bias in two or more domains and ten trials had a high risk of bias due to lack of blinding (placebo was not used in the control arm. Overall, the certainty of evidence was moderate to high, but it was downgraded for IVH due to indirectness; for developmental delay due to risk of bias and for maternal adverse outcomes (death, chorioamnionitis and endometritis) due to imprecision.

Neonatal/child outcomes. Antenatal corticosteroids reduce the risk of:. - perinatal death (risk ratio (RR) 0.85, 95% confidence interval (CI) 0.77 to 0.93; 9833 infants; 14 studies; high-certainty evidence; 2.3% fewer, 95% CI 1.1% to 3.6% fewer),. - neonatal death (RR 0.78, 95% CI 0.70 to 0.87; 10,609 infants; 22 studies; high-certainty evidence; 2.6% fewer, 95% CI 1.5% to 3.6% fewer),. - respiratory distress syndrome (RR 0.71, 95% CI 0.65 to 0.78; 11,183 infants; studies = 26; high-certainty evidence; 4.3% fewer, 95% CI 3.2% to 5.2% fewer). Antenatal corticosteroids probably reduce the risk of IVH (RR 0.58, 95% CI 0.45 to 0.75; 8475 infants; 12 studies; moderate-certainty evidence; 1.4% fewer, 95% CI 0.8% to1.8% fewer), and probably have little to no effect on birthweight (mean difference (MD) -14.02 g, 95% CI -33.79 to 5.76; 9551 infants; 19 studies; high-certainty evidence). Antenatal corticosteroids probably lead to a reduction in developmental delay in childhood (RR 0.51, 95% CI 0.27 to 0.97; 600 children; 3 studies; moderate-certainty evidence; 3.8% fewer, 95% CI 0.2% to 5.7% fewer). Maternal outcomes. Antenatal corticosteroids probably result in little to no difference in maternal death (RR 1.19, 95% CI 0.36 to 3.89; 6244 women; 6 studies; moderate-certainty evidence; 0.0% fewer, 95% CI 0.1% fewer to 0.5% more), chorioamnionitis (RR 0.86, 95% CI 0.69 to 1.08; 8374 women; 15 studies; moderate-certainty evidence; 0.5% fewer, 95% CI 1.1% fewer to 0.3% more), and endometritis (RR 1.14, 95% CI 0.82 to 1.58; 6764 women; 10 studies; moderate-certainty; 0.3% more, 95% CI 0.3% fewer to 1.1% more). The wide 95% CIs in all of these outcomes include possible benefit and possible harm. Authors' conclusions: Evidence from this updated review supports the continued use of a single course of antenatal corticosteroids to accelerate fetal lung maturation in women at risk of preterm birth. Treatment with antenatal corticosteroids reduces the risk of perinatal death, neonatal death and RDS and probably reduces the risk of IVH. This evidence is robust, regardless of resource setting (high, middle or low). Further research should focus on variations in the treatment regimen, effectiveness of the intervention in specific understudied subgroups such as multiple pregnancies and other high-risk obstetric groups, and the risks and benefits in the very early or very late preterm periods. Additionally, outcomes from existing trials with follow-up into childhood and adulthood are needed in order to investigate any longer-term effects of antenatal corticosteroids. We encourage authors of previous studies to provide further information which may answer any remaining questions about the use of antenatal corticosteroids without the need for further randomised controlled trials. Individual patient data meta-analyses from published trials are likely to provide answers for most of the remaining clinical uncertainties.
AU - McGoldrick, Emma
AU - Stewart, Fiona
AU - Parker, Roses
AU - Dalziel, Stuart R.
DA - 2020/12//
DO - 10.1002/14651858.CD004454.pub4
IS - 2
PB - John Wiley and Sons Ltd
PY - 2020
TI - Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth
T2 - Cochrane Database of Systematic Reviews

VL - 2021
ER -
TY - JOUR
AB - Dexamethasone (DEX) was applied in neonatal respiratory distress syndrome treatment of pregnant women. We established a pharmacokinetics (PK)/pharmacodynamics(PD)/end point model of pregnant animals based on published data and then extrapolated to simulate fetal exposure and lung maturation in pregnant women. We first established the PK/PD/end point model for DEX in pregnant sheep. We considered the competitive effect of cortisol (Cort) and DEX binding with glucocorticoid receptor and then used the indirect response model to describe disaturated-phosphatidylcholine (DSPC) dynamics. Based on that, we established a regression relationship between DSPC and fetal lung volume (V40). We then extrapolated the PD/end point model of pregnant sheep to pregnant monkeys by corrected stages of morphologic lung maturation in two species. Finally, we utilized the interspecies extrapolation strategy to simulate fetal exposure (AUC0-48h) and V40 relationship in pregnant women. The current model could well describe the maternal-fetal PK of DEX in pregnant animals. Simulated DEX AUC0-24h values of the umbilical venous to maternal plasma ratio in pregnant sheep and monkeys were 0.31 and 0.27, respectively. The simulated Cort curve and V40 in pregnant sheep closely matched the observed data within a 2-fold range. For pregnant monkeys, model-simulated V40 were well fitted with external verification data, which showed good interspecies extrapolation performance. Finally, we simulated fetal exposure-response relationship in pregnant women, which indicated that the fetal AUC0-48h of DEX should not be less than 300 and 100 ng/mL·hr at GW28 and GW34 to ensure fetal lung maturity. The current model preliminarily provided support for clinical DEX dose optimization.
AU - Song, Ling
AU - Song, Jie
AU - Wang, Ying
AU - Wei, Yuan
AU - Zhao, Yangyu
AU - Liu, Dongyang
DA - 2024/6//
DO - 10.1021/acsptsci.3c00391
IS - 6
KW - DEX
KW - PK/PD/end point model
KW - fetal lung maturation
KW - pregnant women
PB - American Chemical Society
PY - 2024
SP - 1770
EP - 1782
TI - Systematic Quantitative Analysis of Fetal Dexamethasone Exposure and Fetal Lung Maturation in Pregnant Animals: Model Informed Dexamethasone Precision Dose Study
T2 - ACS Pharmacology and Translational Science
VL - 7
ER -
TY - GEN

AU - Vidaeff, Alex C.
AU - Belfort, Michael A.
AU - Kemp, Matthew W.
AU - Saade, George R.
AU - Caughey, Aaron B.
AU - Wapner, Ronald J.
AU - Goldenberg, Robert L.
AU - Jobe, Alan H.
DA - 2023/2//
DO - 10.1016/j.ajog.2022.10.002
IS - 2
PB - Elsevier Inc.
PY - 2023
SP - 129
EP - 132
TI - Updating the balance between benefits and harms of antenatal corticosteroids
T2 - American Journal of Obstetrics and Gynecology
VL - 228
ER -
TY - JOUR
AB - Key content: Antenatal corticosteroids (ACS) are a key evidence-based intervention proven to reduce neonatal morbidity and mortality. ACS should be given in a timely manner to ensure maximal benefit. This can be challenging, particularly in women presenting with suspected spontaneous preterm labour. There is continuing uncertainty about the role of repeat ACS courses in women who remain at high risk of preterm delivery. Evidence from long-term follow-up studies has yielded mixed findings; further research is needed to determine the impact of ACS on future health. Learning objectives: To understand the mechanisms underpinning ACS effectiveness in utero and the evidence to support their use. To understand the rationale for ACS use in specific circumstances, as well as current areas of uncertainty. Ethical issues: For women who receive ACS for threatened preterm labour, there is only benefit if their baby is born within 7 days. Therefore, optimal prediction of risk of preterm delivery is essential. Evidence of benefit of ACS does not translate directly from high-income settings into low- and middle-income countries because there are other factors that influence preterm birth outcomes. Timing of ACS, in relation to time before delivery, number of courses and gestational age, is likely to be important.
AU - Busuulwa, Paula
AU - Groom, Katie
AU - Chappell, Lucy C
AU - Shennan, Andrew H
DA - 2021/10//
DO - 10.1111/tog.12768
IS - 4
PB - Wiley
PY - 2021
SP - 246
EP - 257
TI - The role of antenatal corticosteroids in improving neonatal outcomes

T2 - The Obstetrician & Gynaecologist
VL - 23
ER -
TY - JOUR
AU - Akl, Elie A
AU - Khabsa, Joanne
AU - Iannizzi, Claire
AU - Piechotta, Vanessa
AU - Kahale, Lara A
AU - Barker, James M
AU - McKenzie, Joanne E
AU - Page, Matthew J
AU - Skoetz, Nicole
DA - 2024/11//
DO - 10.1136/bmj-2024-079183
PY - 2024
SP - e079183
EP - e079183
TI - Extension of the PRISMA 2020 statement for living systematic reviews (PRISMA-LSR): checklist and explanation
T2 - BMJ
UR - https://www.bmj.com/lookup/doi/10.1136/bmj-2024-079183
ER -
TY - JOUR
AB - Background: Synthesis of multiple randomized controlled trials (RCTs) in a systematic review can summarize the effects of individual outcomes and provide numerical answers about the effectiveness of interventions. Filtering of searches is time consuming, and no single method fulfills the principal requirements of speed with accuracy. Automation of systematic reviews is driven by a necessity to expedite the availability of current best evidence for policy and clinical decision-making. We developed Rayyan (http://rayyan.qcri.org), a free web and mobile app, that helps expedite the initial screening of abstracts and titles using a process of semi-automation while incorporating a high level of usability. For the beta testing phase, we used two published Cochrane reviews in which included studies had been selected manually. Their searches, with 1030 records and 273 records, were uploaded to Rayyan. Different features of Rayyan were tested using these two reviews. We also conducted a survey of Rayyan's users and collected feedback through a built-in feature. Results: Pilot testing of Rayyan focused on usability, accuracy against manual methods, and the added value of the prediction feature. The "taster" review (273 records) allowed a quick overview of Rayyan for early comments on usability. The second review (1030 records) required several iterations to identify the previously identified 11 trials. The "suggestions" and "hints," based on the "prediction model," appeared as testing progressed beyond five included studies. Post rollout user experiences and a reflexive response by the developers enabled real-time modifications and improvements. The survey respondents reported 40% average time savings when using Rayyan compared to others tools, with 34% of the respondents reporting more than 50% time savings. In addition, around 75% of the respondents mentioned that screening and labeling studies as well as collaborating on reviews to be the two most important features of Rayyan. As of November 2016, Rayyan users exceed 2000 from over 60 countries

conducting hundreds of reviews totaling more than 1.6M citations. Feedback from users, obtained mostly through the app web site and a recent survey, has highlighted the ease in exploration of searches, the time saved, and simplicity in sharing and comparing include-exclude decisions. The strongest features of the app, identified and reported in user feedback, were its ability to help in screening and collaboration as well as the time savings it affords to users. Conclusions: Rayyan is responsive and intuitive in use with significant potential to lighten the load of reviewers.
AU - Ouzzani, Mourad
AU - Hammady, Hossam
AU - Fedorowicz, Zbys
AU - Elmagarmid, Ahmed
DA - 2016/12//
DO - 10.1186/s13643-016-0384-4
IS - 1
KW - Automation
KW - Evidence-based medicine
KW - Systematic reviews
PB - BioMed Central Ltd.
PY - 2016
TI - Rayyan-a web and mobile app for systematic reviews
T2 - Systematic Reviews
VL - 5
ER -
TY - RPRT
AB - Key Points: • Cochrane Overviews of Reviews (Overviews) use explicit and systematic methods to search for and identify multiple systematic reviews on related research questions in the same topic area for the purpose of extracting and analysing their results across important outcomes. • Overviews are similar to reviews of interventions, but the unit of searching, inclusion and data analysis is the systematic review rather than the primary study. • Overviews can describe the current body of systematic review evidence on a topic of interest, or they can address a new review question that wasn't a focus in the included systematic reviews. • Overviews can present outcome data exactly as they appear in the included systematic reviews, or they can re-analyse the systematic review outcome data in a way that differs from the analyses conducted in the systematic reviews. • Prior to conducting an Overview, authors should ensure that the Overview format is the best fit for their review question and that they are prepared to address diverse methodological challenges they are likely to encounter. This chapter should be cited as: Pollock M, Fernandes RM, Becker LA, Pieper D, Hartling L.
AU - Pollock, Michelle
AU - Fernandes, Ricardo M
AU - Becker, Lorne A
AU - Pieper, Dawid
AU - Hartling, Lisa
PY - 2024
TI - Cochrane Handbook for Systematic Reviews of Interventions version 6.5 Chapter V: Overviews of Reviews
UR - www.training.cochrane.org/handbook.
ER -

TY - JOUR
AB - Objective To develop ROBIS, a new tool for assessing the risk of bias in systematic reviews (rather than in primary studies). Study Design and Setting We used four-stage approach to develop ROBIS: define the scope, review the evidence base, hold a face-to-face meeting, and refine the tool through piloting. Results ROBIS is currently aimed at four broad categories of reviews mainly within health care settings: interventions, diagnosis, prognosis, and etiology. The target audience of ROBIS is primarily guideline developers, authors of overviews of systematic reviews ("reviews of reviews"), and review authors who might want to assess or avoid risk of bias in their reviews. The tool is completed in three phases: (1) assess relevance (optional), (2) identify concerns with the review process, and (3) judge risk of bias. Phase 2 covers four domains through which bias may be introduced into a systematic review: study eligibility criteria; identification and selection of studies; data collection and study appraisal; and synthesis and findings. Phase 3 assesses the overall risk of bias in the interpretation of review findings and whether this considered limitations identified in any of the phase 2 domains. Signaling questions are included to help judge concerns with the review process (phase 2) and the overall risk of bias in the review (phase 3); these questions flag aspects of review design related to the potential for bias and aim to help assessors judge risk of bias in the review process, results, and conclusions. Conclusions ROBIS is the first rigorously developed tool designed specifically to assess the risk of bias in systematic reviews.
AU - Whiting, Penny
AU - Savović, Jelena
AU - Higgins, Julian P.T.
AU - Caldwell, Deborah M.
AU - Reeves, Barnaby C.
AU - Shea, Beverley
AU - Davies, Philippa
AU - Kleijnen, Jos
AU - Churchill, Rachel
DA - 2016/1//
DO - 10.1016/j.jclinepi.2015.06.005
KW - Evidence
KW - Meta-analysis
KW - Quality
KW - Risk of bias
KW - Systematic review
KW - Tool
PB - Elsevier USA
PY - 2016
SP - 225
EP - 234
TI - ROBIS: A new tool to assess risk of bias in systematic reviews was developed
T2 - Journal of Clinical Epidemiology
VL - 69
ER -
TY - GEN
AB - The internal and external environment of the mother during the developmental

stages of the fetus affects the offspring’s health. According to the developmental origins of health and disease (DOHaD) theory, environmental factors influence the offspring and also affect health in adulthood. Recently, studies based on this theory have gained attracted attention because of their clinical utility in identifying the risk groups for various diseases. Neurodevelopmental disorders (NDDs) such as autism spectrum disorder (ASD) and attention-deficit hyperactivity disorder (ADHD) can be caused by exposure to certain prenatal environments during pregnancy. This review describes the latest findings on the effect of prenatal environment on the onset mechanism of NDDs based on the DOHaD theory. Unravelling the molecular mechanisms underlying the pathogenesis of NDDs is important, because there are no therapeutic drugs for these disorders. Furthermore, elucidating the relationship between the DOHaD theory and NDDs will contribute to the popularization of preventive medicine.
AU - Doi, Miyuki
AU - Usui, Noriyoshi
AU - Shimada, Shoichi
DA - 2022/3//
DO - 10.3389/fendo.2022.860110
KW - DOHaD
KW - autism spectrum disorder (ASD)
KW - low birth weight (LBW)
KW - neurodevelopmental disorders (NDDs)
KW - prenatal environment
KW - preterm birth (PTB)
PB - Frontiers Media S.A.
PY - 2022
TI - Prenatal Environment and Neurodevelopmental Disorders
T2 - Frontiers in Endocrinology
VL - 13
ER -
TY - GEN
AB - Prenatal exposure to maternal immune activation (MIA) is a risk factor for a variety of neurodevelopmental and psychiatric disorders. The timing of MIA-exposure has been shown to affect adolescent and adult offspring neurodevelopment, however, less is known about these effects in the neonatal period. To better understand the impact of MIA-exposure on neonatal brain development, we first assess neonate communicative abilities with the ultrasonic vocalization task, followed by high-resolution <italic>ex vivo</italic> magnetic resonance imaging (MRI) on the neonatal (postnatal day 8) brain. Early exposed offspring displayed decreased communicative ability, while brain anatomy appeared largely unaffected, apart from some subtle alterations. By integrating MRI and behavioural assays to investigate the effects of MIA-expsoure on neonatal neurodevelopment we show that offspring neuroanatomy and behaviour are only subtly affected by both early and late exposure. This suggests that the deficits often observed in later stages of life may be dormant, not yet developed in the neonatal period, or not as easily detectable using a cross-sectional approach.
AU - Guma, Elisa
AU - Snook, Emily
AU - Spring, Shoshana
AU - Lerch, Jason P.

AU - Nieman, Brian J.
AU - Devenyi, Gabriel A.
AU - Chakravarty, M. Mallar
DA - 2021/8//
DO - 10.1101/2021.08.12.456095
PY - 2021
TI - Subtle alterations in neonatal neurodevelopment following early or late exposure to prenatal maternal immune activation
UR - http://biorxiv.org/lookup/doi/10.1101/2021.08.12.456095
ER -
TY - JOUR
AB - The prenatal period represents a critical time for brain growth and development. These rapid neurological advances render the fetus susceptible to various influences with life-long implications for mental health. Maternal distress signals are a dominant early life influence, contributing to birth outcomes and risk for offspring psychopathology. This prospective longitudinal study evaluated the association between prenatal maternal distress and infant white matter microstructure. Participants included a racially and socioeconomically diverse sample of 85 mother-infant dyads. Prenatal distress was assessed at 17 and 29 weeks' gestational age (GA). Infant structural data were collected via diffusion tensor imaging (DTI) at 42-45 weeks' postconceptional age. Findings demonstrated that higher prenatal maternal distress at 29 weeks' GA was associated with increased fractional anisotropy, b =.283, t(64) = 2.319, p =.024, and with increased axial diffusivity, b =.254, t(64) = 2.067, p =.043, within the right anterior cingulate white matter tract. No other significant associations were found with prenatal distress exposure and tract fractional anisotropy or axial diffusivity at 29 weeks' GA, or earlier in gestation.
AU - Demers, Catherine H.
AU - Bagonis, Maria M.
AU - Al-Ali, Khalid
AU - Garcia, Sarah E.
AU - Styner, Martin A.
AU - Gilmore, John H.
AU - Hoffman, M. Camille
AU - Hankin, Benjamin L.
AU - Davis, Elysia Poggi
DA - 2021/12//
DO - 10.1017/S0954579421000742
IS - 5
KW - anxiety
KW - diffusion tensor imaging (DTI)
KW - magnetic resonance imaging (MRI)
KW - pregnancy
KW - white matter microstructure
PB - Cambridge University Press
PY - 2021
SP - 1526
EP - 1538
TI - Exposure to prenatal maternal distress and infant white matter neurodevelopment

T2 - Development and Psychopathology
VL - 33
ER -
TY - JOUR
AB - Background: Prenatal phthalate exposure has been linked with altered neurodevelopment, including externalizing behaviors and attention-deficit hyperactivity disorder (ADHD). However, the implicated metabolite, neurobehavioral endpoint, and child sex have not always been consistent across studies, possibly due to heterogeneity in neurodevelopmental instruments. The complex set of findings may be synthesized using executive function (EF), a construct of complex cognitive processes that facilitate ongoing goal-directed behaviors. Impaired EF can be presented with various phenotypes of poor neurodevelopment, differently across structured conditions, home/community, or preschool/school. We evaluated the relationship between prenatal phthalate exposure and comprehensive assessment of preschool EF. Methods: Our study comprised 262 children with clinically significant/subthreshold ADHD symptoms and 78 typically developing children who were born between 2003 and 2008 and participated in the Preschool ADHD Substudy, which is nested within a population-based prospective cohort study, the Norwegian Mother, Father, and Child Cohort (MoBa). Twelve phthalate metabolites were measured from urine samples that their mothers had provided during pregnancy, at 17 weeks' gestation. All children, at approximately 3.5-years, took part in a detailed clinical assessment that included parent-and teacher-rated inventories and administered tests. We used instruments that measured constructs related to EF, which include a parent-and teacher-reported Behavior Rating Inventory of Executive Function-Preschool (BRIEF-P) and three performance-based tests: A Developmental NEuroPSYchological Assessment (NEPSY), Stanford-Binet intelligence test V (SB5), and the cookie delay task (CDT). The standard deviation change in test score per interquartile range (IQR) increase in phthalate metabolite was estimated with multivariable linear regression. We applied weighting in all models to account for the oversampling of children with clinically significant or subthreshold symptoms of ADHD. Additionally, we assessed modification by child sex and potential co-pollutant confounding. Results: Elevated exposure to mono-benzyl phthalate (MBzP) during pregnancy was associated with poorer EF, across all domains and instruments, in both sex. For example, an IQR increase in MBzP was associated with poorer working memory rated by parent (1.23 [95% CI: 0.20, 2.26]) and teacher (1.13 [0.14, 2.13]) using BRIEF-P, and administered tests such as SB5 (no-verbal: 0.19 [0.09, 0.28]; verbal: 0.13 [0.01, 0.25]). Adverse associations were also observed for mono-n-butyl phthalate (MnBP) and mono-iso-butyl phthalate (MiBP), although results varied by instruments. EF domains reported by parents using BRIEF-P were most apparently implicated, with stronger associations among boys (e.g., MnBP and inhibition: 2.74 [1.77, 3.72]; MiBP and inhibition: 1.88 [0.84, 2.92]) than among girls (e.g., MnBP and inhibition: −0.63 [−2.08, 0.83], interaction p-value: 0.04; MiBP and inhibition: −0.15 [−1.04, 0.74], interaction p-value: 0.3). Differences by sex, however, were not found for the teacher-rated BRIEF-P or administered tests including NEPSY, SB5, and CDT. Conclusion and relevance: Elevated mid-pregnancy MBzP, MiBP, and MnBP were associated with more adverse profiles of EF among preschool-aged children across a range of instruments and raters, with some associations found only among boys. Given our findings and accumulating evidence of the prenatal period as a critical window for phthalate exposure, there is a timely need to expand the current phthalate regulations focused on baby products to

include pregnancy exposures.
AU - Choi, Giehae
AU - Villanger, Gro D.
AU - Drover, Samantha S.M.
AU - Sakhi, Amrit K.
AU - Thomsen, Cathrine
AU - Nethery, Rachel C.
AU - Zeiner, Pål
AU - Knudsen, Gun Peggy
AU - Reichborn-Kjennerud, Ted
AU - Øvergaard, Kristin R.
AU - Herring, Amy H.
AU - Skogan, Annette H.
AU - Biele, Guido
AU - Aase, Heidi
AU - Engel, Stephanie M.
DA - 2021/4//
DO - 10.1016/j.envint.2021.106403
KW - Benzyl-phthalates
KW - Butyl-phthalates
KW - Executive function
KW - MoBa
KW - Neurodevelopment
KW - Phthalates
PB - Elsevier Ltd
PY - 2021
TI - Prenatal phthalate exposures and executive function in preschool children
T2 - Environment International
VL - 149
ER -
TY - JOUR
AB - Background: Higher prenatal ambient air pollution exposure has been associated with impaired neurodevelopment in preschoolers and school-aged children. The purpose of this study was to explore the relationships between prenatal ambient air pollution exposure and neurodevelopment during infancy. Methods: This study examined 161 Latino mother-infant pairs from the Southern California Mother’s Milk Study. Exposure assessments included prenatal nitrogen dioxide (NO2) and particulate matter smaller than 2.5 and 10 microns in diameter (PM2.5 and PM10, respectively). The pregnancy period was also examined as three windows, early, mid, and late, which describe the first, middle, and last three months of pregnancy. Infant neurodevelopmental outcomes at 2 years of age were measured using the Bayley-III Scales of Infant and Toddler Development. Multivariable linear models and distributed lag linear models (DLM) were used to examine relationships between prenatal exposures and neurodevelopmental scores, adjusting for socioeconomic status, breastfeeding frequency, time of delivery, pre-pregnancy body mass index, and infant birthweight and sex. Results: Higher prenatal exposure to PM10 and PM2.5 was negatively associated with composite cognitive score (β = -2.01 [-3.89, -0.13] and β = -1.97 [-3.83, -0.10], respectively). In addition, higher average prenatal exposure to PM10 was negatively associated with composite motor (β = -2.35 [-3.95, -0.74]), scaled motor (β = -0.77 [-1.30, -0.24]), gross motor (β = -0.37 [-0.70,

-0.04]), fine motor (β = -0.40 [-0.71, -0.09]), composite language (β = -1.87 [-3.52, -0.22]), scaled language (β = -0.61 [-1.18, -0.05]) and expressive communication scaled scores (β = -0.36 [-0.66, -0.05]). DLMs showed that higher prenatal air pollution exposure during mid and late pregnancy was inversely associated with motor, cognitive, and communication language scores. Conclusions: Higher exposure to air pollutants during pregnancy, particularly in the mid and late prenatal periods, was inversely associated with scaled and composite motor, cognitive, and language scores at 2 years. These results indicate that prenatal ambient air pollution may negatively impact neurodevelopment in early life.
AU - Morgan, Zachariah E.M.
AU - Bailey, Maximilian J.
AU - Trifonova, Diana I.
AU - Naik, Noopur C.
AU - Patterson, William B.
AU - Lurmann, Frederick W.
AU - Chang, Howard H.
AU - Peterson, Bradley S.
AU - Goran, Michael I.
AU - Alderete, Tanya L.
DA - 2023/12//
DO - 10.1186/s12940-022-00951-y
IS - 1
KW - Air Pollution
KW - Child Development
KW - Health Disparities
KW - Neurodevelopment
KW - Pregnancy Exposures
PB - BioMed Central Ltd
PY - 2023
TI - Prenatal exposure to ambient air pollution is associated with neurodevelopmental outcomes at 2 years of age
T2 - Environmental Health: A Global Access Science Source
VL - 22
ER -
TY - JOUR
AB - Prenatal cannabis exposure (PCE) is of increasing concern globally, due to the potential impact on offspring neurodevelopment, and its association with childhood and adolescent brain development and cognitive function. However, there is currently a lack of research addressing the molecular impact of PCE, that may help to clarify the association between PCE and neurodevelopment. To address this knowledge gap, here we present epigenome-wide association study data across multiple time points, examining the effect of PCE and co-exposure with tobacco using two longitudinal studies, the Avon Longitudinal Study of Parents and Children (ALSPAC) and the Christchurch Health and Development Study (CHDS) at birth (0 y), 7 y and 15-17 y (ALSPAC), and ~27 y (CHDS). Our findings reveal genome-wide significant DNA methylation differences in offspring at 0 y, 7 y, 15-17 y, and 27 y associated with PCE alone, and co-exposure with tobacco. Importantly, we identified significantly differentially methylated CpG sites within the genes LZTS2, NPSR1, NT5E, CRIP2, DOCK8, COQ5, and LRP5 that are shared between different time points throughout development in offspring. Notably, functional pathway analysis showed

enrichment for differential DNA methylation in neurodevelopment, neurotransmission, and neuronal structure pathways, and this was consistent across all timepoints in both cohorts. Given the increasing volume of epidemiological evidence that suggests a link between PCE and adverse neurodevelopmental outcomes in exposed offspring, this work highlights the need for further investigation into PCE, particularly in larger cohorts.
AU - Noble, Alexandra J
AU - Adams, Alex T
AU - Satsangi, Jack
AU - Boden, Joseph M
AU - Osborne, Amy J
DA - 2024/9//
DO - 10.1038/s41380-024-02752-w
PY - 2024
TI - Prenatal cannabis exposure is associated with alterations in offspring DNA methylation at genes involved in neurodevelopment, across the life course.
T2 - Molecular psychiatry
UR - http://www.ncbi.nlm.nih.gov/pubmed/39277688
ER -
TY - GEN
AB - Preeclampsia, a hypertensive disorder during pregnancy, frequently correlates with adverse neurological outcomes in offspring, including cognitive impairments, autism spectrum disorder, depressive disorder, attention deficit hyperactivity disorder, and cerebral palsy. Despite these known consequences, the understanding of neuronal damage in the offspring of preeclamptic mothers remains insufficient. Here, we review the neuronal abnormalities resulting from maternal preeclampsia exposure, which include disrupted neurogenesis, loss of neuronal cell integrity, accumulation of cellular debris, decreased synaptogenesis and myelination, and increased neurite growth stimulated by maternal preeclampsia serum. The underlying mechanisms potentially driving these effects involve microglial activation, inflammatory responses, and reduced angiogenesis. Intervention strategies aimed at improving fetal neuronal outcomes are also discussed, encompassing pharmacological treatments such as pravastatin, tadalafil, and melatonin, as well as non-pharmacological approaches like dietary modifications, maternal exercise, and standard care for children. These interventions hold promise for clinical application, offering avenues to address early neuronal abnormalities and prevent the onset of long-term neurological disorders.
AU - Zhang, He
AU - Lin, Jinju
AU - Zhao, Huashan
DA - 2024/10//
DO - 10.3390/ijms252011062
IS - 20
KW - intervention
KW - neurological outcomes
KW - neuronal abnormalities
KW - offspring
KW - preeclampsia
PB - Multidisciplinary Digital Publishing Institute (MDPI)
PY - 2024

TI - Impacts of Maternal Preeclampsia Exposure on Offspring Neuronal Development: Recent Insights and Interventional Approaches
T2 - International Journal of Molecular Sciences
VL - 25
ER -
TY - JOUR
AB - Background: It has been well recognized that antenatal administration of dexamethasone to pregnant women at risk of preterm delivery may markedly accelerate fetal maturation and reduce the risk of adverse perinatal outcomes in their preterm infants, particularly for births before 34 weeks of gestation. Since 2015, antenatal corticosteroid administration has been extended beyond 34 weeks of gestation by clinical guidelines, as it might have beneficial effects on fetal maturation and perinatal outcomes. However, concerns regarding the potential influence of antenatal corticosteroid treatment on offspring neurodevelopment have been raised. Objective: This study aimed to investigate whether maternal antenatal corticosteroid administration was associated with neurodevelopment in infants at 1 year of age. Study Design: In this prospective and longitudinal birth cohort study, women were followed up throughout gestation, and their infants underwent a Bayley Scales of Infant and Toddler Development, Third Edition, screening test at 1 year of age between December 2018 and September 2020. Finally, 1609 pregnant women and 1759 infants were included in the current study. Using a generalized linear mixed model, we examined the association between antenatal corticosteroid exposure and infant neurodevelopment in cognitive, receptive communication, expressive communication, fine motor, and gross motor functions. Results: Of the 1759 infants eligible for this study, 1453 (82.6%) were singletons. A total of 710 infants were exposed to antenatal corticosteroids, among whom 415 were dexamethasone exposed and 483 were prednisone exposed. Dexamethasone was prescribed most often in late pregnancy, whereas prednisone was often used before 8 weeks of gestation among women who conceived through assisted reproductive technology. Compared with those who had no exposure, antenatal corticosteroid exposure was associated with an increased risk of infants being noncompetent in the cognitive development domain after adjusting for conventional risk factors (adjusted risk ratio, 1.53; 95% confidence interval, 1.08–2.18; P=.017). For medication-specific exposure, those exposed vs not exposed to antenatal dexamethasone were 1.62-fold (95% confidence interval, 1.10–2.38; P=.014) more likely to be noncompetent in the cognitive development domain at 1 year. The association did not vary markedly between preterm and term infants, singletons and twins, or assisted reproductive technology–conceived and spontaneously conceived infants (all P>.05 for heterogeneity). In contrast, a null association was observed for the risk of being noncompetent in any domain of neurodevelopment with antenatal prednisone exposure at early pregnancy. Conclusion: Here, antenatal corticosteroid, particularly dexamethasone exposure, was markedly associated with an increased risk of infants being noncompetent in the cognitive development domain at 1 year of age. These findings may provide new information when weighing the benefits and potential risks of maternal antenatal corticosteroid administration.
AU - Tao, Shiyao
AU - Du, Jiangbo
AU - Chi, Xia
AU - Zhu, Yeyi
AU - Wang, Xiaoyan

AU - Meng, Qingxia
AU - Ling, Xiufeng
AU - Diao, Feiyang
AU - Song, Ci
AU - Jiang, Yangqian
AU - Lv, Hong
AU - Lu, Qun
AU - Qin, Rui
AU - Huang, Lei
AU - Xu, Xin
AU - Liu, Cong
AU - Ding, Yuqing
AU - Jiang, Tao
AU - Ma, Hongxia
AU - Xia, Yankai
AU - Liu, Jiayin
AU - Lin, Yuan
AU - Jin, Guangfu
AU - Hu, Zhibin
DA - 2022/11//
DO - 10.1016/j.ajog.2022.05.060
IS - 5
KW - 1 year old
KW - antenatal dexamethasone
KW - antenatal prednisone
KW - cognitive
KW - expressive communication
KW - fine motor
KW - gross motor
KW - intrauterine exposure
KW - receptive communication
PB - Elsevier Inc.
PY - 2022
SP - 759.e1
EP - 759.e15
TI - Associations between antenatal corticosteroid exposure and neurodevelopment in infants
T2 - American Journal of Obstetrics and Gynecology
VL - 227
ER -
TY - GEN
AB - Despite advances in neonatal intensive care, survivors of premature birth remain highly susceptible to unique patterns of developmental brain injury that manifest as cerebral palsy and cognitive-learning disabilities. The developing brain is particularly susceptible to cerebral white matter injury related to hypoxia-ischemia. Cerebral white matter development in fetal sheep shares many anatomical and physiological similarities with humans. Thus, the fetal sheep has provided unique experimental access to the complex pathophysiological processes that contribute to injury to the human brain during successive periods in development. Recent refinements have resulted in models that replicate major

features of acute and chronic human cerebral injury and have provided access to complex clinically relevant studies of cerebral blood flow and neuroimaging that are not feasible in smaller laboratory animals. Here, we focus on emerging insights and methodologies from studies in fetal sheep that have begun to define cellular and vascular factors that contribute to white matter injury. Recent advances include spatially defined measurements of cerebral blood flow in utero, the definition of cellular maturational factors that define the topography of injury and the application of high-field magnetic resonance imaging to define novel neuroimaging signatures for specific types of chronic white matter injury. Despite the higher costs and technical challenges of instrumented preterm fetal sheep models, they provide powerful access to clinically relevant studies that provide a more integrated analysis of the spectrum of insults that appear to contribute to cerebral injury in human preterm infants.
AU - Back, Stephen A.
AU - Riddle, Art
AU - Dean, Justin
AU - Hohimer, A. Roger
DA - 2012/4//
DO - 10.1007/s13311-012-0108-y
IS - 2
KW - Cerebral blood flow
KW - Cerebral palsy
KW - Hypoxia-ischemia
KW - MRI
KW - Myelin
KW - Oligodendrocyte
KW - Ovine
KW - White matter
PY - 2012
SP - 359
EP - 370
TI - The Instrumented Fetal Sheep as a Model of Cerebral White Matter Injury in the Premature Infant
T2 - Neurotherapeutics
VL - 9
ER -
TY - RPRT
AB - Neurotoxic effects of prenatal administration of dexamethasone were examined in the fetal rhesus monkey brain at 135 and 162 days of gestation (term is 165 days). In an experimental design mimicking human clinical trials, dexamethasone was given intramuscularly to pregnant monkeys on day 132 (single injection with doses of 0.5, 5, or 10 mg/kg maternal body weight) or on days 132 and 133 (multiple injections at 12-h intervals with 0.125 × 4, 1.25 × 4, or 2.5 mg/kg × 4). The fetuses were delivered by caesarean section on day 135 or day 162 and hippocampal slices were prepared for evaluation. Light and electron microscopic observation revealed decreased numbers of pyramidal neurons in the hippocampal CA regions and of granular neurons in the dentate gyrus associated with degeneration of neuronal perikarya and dendrites. Axodendritic synaptic terminals of the mossy fibers in the CA3 hippocampal region showed pronounced degeneration. Degeneration was

dose-dependent and multiple injections induced more severe damage than single injections of the same total dose. Even the lowest dose (0.5 mg/kg, which is similar to the dose used in human clinical trials) produced these changes. Degenerative changes induced by dexamethasone treatment (5 mg/kg) on days 132 and 133 were also clearly evident in fetuses studied at 162 days. Therefore, caution is recommended in the use of prenatal corticosteroids in premature deliveries.
AU - Uno ~', Hideo
AU - Lohmiller, Lon
AU - Thieme, Carol
AU - Kemnitz, Joseph W
AU - Engle, Michael J
AU - Roecker, Ellen B
AU - Farrell, Philip M
KW - Dexamethasone
KW - Fetus
KW - Hippocampus
KW - Neurotoxicity
KW - Prenatal treatment
KW - Respiratory distress syndrome
KW - Rhesus monkey
PY - 1990
SP - 157
EP - 167
TI - Brain damage induced by prenatal exposure to dexamethasone in fetal rhesus macaques. I. Hippocampus
T2 - Developmental Brain Research
VL - 53
ER -
TY - RPRT
AB - Maternal administration of corticosteroids is used to promote lung maturation in human infants considered at risk of preterm delivery [1]. Randomised trials of a single course of corticosteroid treatment have indicated no adverse long-term neurological or cognitive sequelae [2-5]. However, the current trend in many obstetric centres is to use repeated courses in cases where preterm birth has not eventuated, but the risk persists 7 days beyond administration of the original course [6-7]. This practice has not yet been subject to randomised trials of outcome. We have examined the effect of repeated injections of corticosteroids on the development of the optic nerve in prenatal fetal sheep and report a significant delay in the myelination of optic axons. Our results, together with those from other animal studies [8], show that repeated courses of corticosteroids may be detrimental to central nervous system (CNS) development. Clinical practice should balance the known beneficial effects on lung maturation of a single course of corticosteroid against the potential damage to the CNS of repeated courses.
AU - Dunlop, Sarah A
AU - Archer Bsc, Michael A
AU - Quinlivan, Julie A
AU - Beazley, Lyn D
AU - Newnham, John P
KW - corticosteroids
KW - fetus

KW - maturation
KW - myelination
KW - sheep
PB - Wiley-Liss, Inc
PY - 1997
SP - 309
EP - 313
TI - Repeated Prenatal Corticosteroids Delay Myelination in the Ovine Central Nervous System
T2 - J. Matern.-Fetal Med
VL - 6
ER -
TY - RPRT
AB - Objective: To compare the effects of single and repeated courses of corticosteroids on brain growth in fetal sheep. Methods: Pregnant sheep were given intramuscular beta-methasone (0.5 mg/kg) at 104 days' gestation followed at 111, 118, and 124 days by equivalent volumes of sterile normal saline (n 12) or betamethasone (n 12). Controls received equivalent volumes of sterile normal saline at all four intervals (n 12). Lambs were delivered at 125 (preterm) or 145 (term) days. After perfusion, we measured weights (grams) for whole brain, cerebrum, cerebellum, and brain stem, volumes (milliliters) for whole brain and cerebrum, and maximum cerebral anterior-posterior length, width, and depth (centimeters). Results: In the single-injection group at preterm, there were no significant differences (P .070) in whole-brain weight between the corticosteroid-treated animals (38.0 1.81 g) and controls (42.5 1.65 g). Cerebral length and depth were significantly reduced in the corticosteroid group (P < < < .05); other measures were not significantly different. At term, whole-brain weight was significantly lower (47.5 1.70 g; P .022) compared with controls (53.4 1.73 g). All other measures were significantly reduced (P < < < .05) except cerebral and brain-stem weights and cerebral length. In the group that received repeated injections at preterm, whole-brain weight was significantly reduced (35.5 1.65 g; P .005) compared with controls (42.5 1.65 g). All other measures were significantly reduced (P < < < .05) except cere-bellar and brain-stem weights. At term, whole-brain weight was also significantly reduced (42.4 1.52 g; P .001) compared with controls (53.4 1.73 g) as were all other measures (P < < < .05). Conclusion: Administration of single and repeated courses of corticosteroids to pregnant sheep retarded fetal brain growth. (Obstet Gynecol 1999;94:213-8.
AU - Huang, W L
AU - Beazley, L D
AU - Quinlivan, J A
AU - Evans, S F
AU - Newnham, J P
AU - Dunlop, S A
PY - 1999
TI - Effect of Corticosteroids on Brain Growth in Fetal Sheep
ER -
TY - GEN
AB - Antenatal steroids (ANS) are one of the most widely prescribed medications in pregnancy, being administered to women at risk of preterm delivery. In the setting of preterm delivery at or below 35 weeks' gestation, systematic review data show

ANS reduce perinatal morbidity and mortality, primarily by promoting fetal lung maturation. However, with the expanding use of this intervention has come a growing appreciation for the potential off-target, adverse effects of ANS therapy on wider fetal development. We undertook a narrative literature review of the animal and clinical literature to assess current evidence for adverse effects of ANS exposure and fetal development. This review presents a summary of the evidence relating to the potential for wide-ranging, off-target, adverse effects of ANS therapy on fetal development and programming. We highlight an urgent need for further animal and clinical studies investigating the effects of ANS on the fetal immune, cardiovascular, renal and hepatic systems given a current sparsity of evidence. We also strongly suggest an emphasis on open disclosure, discussion and education of clinicians and patients with regard to the potential benefits and risks of ANS therapy, particularly in late preterm and term gestations where infants derive relatively few benefits from these drugs. We also propose further studies on the optimisation of ANS therapy through improved patient selection and improved dosing regimens based on a pharmacokinetic-pharmacodynamic informed understanding of ANS action on the fetal lung.
AU - Carter, Sean W.D.
AU - Kemp, Matthew W.
DA - 2025/3//
DO - 10.1017/S2040174425000078
KW - Antenatal steroids
KW - HPA axis
KW - adverse effects
KW - cardiovascular
KW - development
KW - fetal
KW - growth restriction
KW - hepatic
KW - immune
KW - neurodevelopment
KW - on and off target
KW - preterm birth
KW - programming
KW - renal
PB - Cambridge University Press
PY - 2025
TI - A review of the potential off-target effects of antenatal steroid exposures on fetal development
T2 - Journal of Developmental Origins of Health and Disease
VL - 16
ER -
TY - JOUR
AB - Objective: The purpose of this study is to clarify the effects on the brain including neurogenesis pretreated with repeated doses of dexamethasone in the neonatal rat. Study design: The 4-day-old Sprague Dawley rats were pretreated with 4 different regimens, namely, single administration of dexamethasone, 2-dose administration, 3-dose administration, and saline administration as a control. Concurrently, bromodeoxyuridine (BrdU), which was incorporated into the dividing cells, was administered. We examined body weight, brain weight, and the number of

BrdU-labeled cells in the subventricular zone (SVZ), the subgranular zone (SGZ), and the cortex. Results: Both the body and brain weight of the rats pretreated with dexamethasone were significantly decreased compared with those given saline. Quantitative analysis of BrdU-labeled cells revealed the significant dose-dependent decreases in the SVZ, the SGZ, and the cortex with the dexamethasone treatment. Conclusion: We concluded that the decreases in neurogenesis caused by repeated antenatal corticosteroid therapy might result in the adverse effects on the size of the head at birth.
AU - Kanagawa, Takeshi
AU - Tomimatsu, Takuji
AU - Hayashi, Shusaku
AU - Shioji, Mitsunori
AU - Fukuda, Hiromitsu
AU - Shimoya, Koichiro
AU - Murata, Yuji
DA - 2006/1//
DO - 10.1016/j.ajog.2005.06.015
IS - 1
KW - Bromodeoxyuridine
KW - Neonatal rat
KW - Neurogenesis
KW - Repeated corticosteroid
PY - 2006
SP - 231
EP - 238
TI - The effects of repeated corticosteroid administration on the neurogenesis in the neonatal rat
T2 - American Journal of Obstetrics and Gynecology
VL - 194
ER -
TY - JOUR
AB - Antenatal administration of synthetic glucocorticoids (sGC) is the standard of care for women at risk for preterm labor before 34 gestational weeks. Despite their widespread use, the type of sGC used and their dose or the dosing regimens are not standardized in the United States of America or worldwide. Several studies have identified neural deficits and the increased risk for cognitive and psychiatric disease later in life for children administered sGC prenatally. However, the precise molecular and cellular targets of GC action in the developing brain remain largely undefined. In this study, we demonstrate that a single dose of glucocorticoid during mid-gestation in mice leads to enhanced proliferation in select cerebral cortical neural stem/progenitor cell populations. These alterations are mediated by dose-dependent changes in the expression of cell cycle inhibitors and in genes that promote cell cycle re-entry. This leads to changes in neuronal number and density in the cerebral cortex at birth, coupled to long-term alterations in neurite complexity in the prefrontal cortex and hippocampus in adolescents, and changes in anxiety and depressive-like behaviors in adults.
AU - Tsiarli, M. A.
AU - Rudine, A.
AU - Kendall, N.
AU - Pratt, M. O.

AU - Krall, R.
AU - Thiels, E.
AU - Defranco, D. B.
AU - Monaghan, A. P.
DA - 2017/6//
DO - 10.1038/TP.2017.65
IS - 6
PB - Springer Nature
PY - 2017
TI - Antenatal dexamethasone exposure differentially affects distinct cortical neural progenitor cells and triggers long-term changes in murine cerebral architecture and behavior
T2 - Translational Psychiatry
VL - 7
ER -
TY - JOUR
AB - Synthetic glucocorticoids are administered to pregnant women at risk for preterm delivery, to enhance fetal lung maturation. The benefit of this treatment is well established, however caution is necessary because of possible unwanted side effects on development of different organ systems, including the brain. Actions of glucocorticoids are mediated by corticosteroid receptors, which are highly expressed in the hippocampus, a brain structure involved in cognitive functions. Therefore, we analyzed the effects of a single antenatal dexamethasone treatment on the development of the mouse hippocampus. A clinically relevant dose of dexamethasone (0.4 mg/kg) was administered to pregnant mice at embryonic day 15.5 and the hippocampus was analyzed from embryonic day 16 until adulthood. We investigated the effects of dexamethasone treatment on anatomical changes, apoptosis and proliferation in the hippocampus, hippocampal volume and on total body weight. Our results show that dexamethasone treatment reduced body weight and hippocampal volume transiently during development, but these effects were no longer detected at adulthood. Dexamethasone treatment increased the number of apoptotic cells in the hippocampus until birth, but postnatally no effects of dexamethasone treatment on apoptosis were found. During the phase with increased apoptosis, dexamethasone treatment reduced the number of proliferating cells in the subgranular zone of the dentate gyrus. The number of proliferative cells was increased at postnatal day 5 and 10, but was decreased again at the adult stage. This latter long-term and negative effect of antenatal dexamethasone treatment on the number of proliferative cells in the hippocampus may have important implications for hippocampal network function. © 2014 Noorlander et al.
AU - Noorlander, Cornelle W.
AU - Tijsseling, Deodata
AU - Hessel, Ellen V.S.
AU - De Vries, Willem B.
AU - Derks, Jan B.
AU - Visser, Gerard H.A.
AU - De Graan, Pierre N.E.
DA - 2014/1//
DO - 10.1371/journal.pone.0085671
IS - 1
PB - Public Library of Science

PY - 2014
TI - Antenatal glucocorticoid treatment affects hippocampal development in mice
T2 - PLoS ONE
VL - 9
ER -
TY - JOUR
AB - Antenatal corticosteroids (ANS) are the major intervention to decrease respiratory distress syndrome and mortality from premature birth and are standard of care. The use of ANS is expanding to include new indications and gestational ages, although the recommended dosing was never optimized. The most widely used treatment is two intramuscular doses of a 1:1 mixture of betamethasone-phosphate (Beta-P) and betamethasone-acetate (Beta-Ac) – the clinical drug. We tested in a primate model the efficacy of the slow release Beta-Ac alone for enhancing fetal lung maturation and to reduce fetal corticosteroid exposure and potential toxic effects. Pregnant rhesus macaques at 127 days of gestation (80% of term) were treated with either the clinical drug (0.25 mg/kg) or Beta-Ac (0.125 mg/kg). Beta-Ac alone increased lung compliance and surfactant concentration in the fetal lung equivalently to the clinical drug. By transcriptome analyses the early suppression of genes associated with immune responses and developmental pathways were less affected by Beta-Ac than the clinical drug. Promoter and regulatory analysis prediction identified differentially expressed genes targeted by the glucocorticoid receptor in the lung. At 5 days the clinical drug suppressed genes associated with neuronal development and differentiation in the fetal hippocampus compared to control, while low dose Beta-Ac alone did not. A low dose ANS treatment with Beta-Ac should be assessed for efficacy in human trials.
AU - Schmidt, Augusto F.
AU - Kannan, Paranthaman S.
AU - Bridges, James P.
AU - Filuta, Alyssa
AU - Lipps, Dakota
AU - Kemp, Matthew
AU - Miller, Lisa A.
AU - Kallapur, Suhas G.
AU - Xu, Yan
AU - Whitsett, Jeffrey A.
AU - Jobe, Alan H.
DA - 2019/12//
DO - 10.1038/s41598-019-45171-6
IS - 1
PB - Nature Publishing Group
PY - 2019
TI - Dosing and formulation of antenatal corticosteroids for fetal lung maturation and gene expression in rhesus macaques
T2 - Scientific Reports
VL - 9
ER -
TY - JOUR
AB - Reference information: JCI Insight. 2022;7(18):e162101. https://doi.org/10.1172/jci. insight.162101.
AU - Schmidt, Augusto F

AU - Schnell, Daniel J
AU - Eaton, Kenneth P
AU - Chetal, Kashish
AU - Kannan, Paranthaman S
AU - Miller, Lisa A
AU - Chougnet, Claire A
AU - Swarr, Daniel T
AU - Jobe, Alan H
AU - Salomonis, Nathan
AU - Kamath-Rayne, Beena D
DO - 10.1172/jci
PY - 2022
TI - Fetal maturation revealed by amniotic fluid cell-free transcriptome in rhesus macaques
UR - https://doi.org/10.1172/jci.
ER -
TY - JOUR
AB - The endogenous glucocorticoid (GC) surge in late gestation plays a vital role in maturation of several organ systems. For this reason, pregnant women at risk of preterm labor are administered synthetic glucocorticoids (sGCs) to promote fetal lung development. Animal studies have shown that fetal sGC exposure can cause life-long changes in endocrine and metabolic function.Wehave previously shown that antenatal sGC treatment is associated with alterations in global DNA methylation and modifications to the hippocampal methylome and acetylome. In this study, we hypothesized that: 1) there are changesin the transcriptional landscape of the fetalhippocampusin late gestation, associated with the endogenous cortisol surge; 2) fetal sGC exposure alters genome-wide transcription in the hippocampus; and 3) these changes in transcription are associated with modified glucocorticoid receptor (GR) DNAbinding andDNAmethylation. sGC was administered as 2 courses on gestational days (GD) 40, 41, 50, and 51, and the hippocampi of fetal guinea pigs were examined before (GD52) and after (GD65) theendogenouscortisol surge (Term~GD67).Wealso analyzed fetal hippocampi 24 hoursand14 days followingmaternalsGCinjections (n=3-4/group).Genome-widemodificationoftranscriptionandGR DNAbindingoccurredin late gestation, in parallelwiththenormalGCsurge. Further,sGCexposurehad a substantial impact on the hippocampal transcriptome, GR-DNA binding, andDNAmethylation at 24 hours and 14 days following the final sGC treatment. These data support the hypothesis that GC exposure in late gestation plays a significant role in modifying the transcriptional and epigenetic landscape of the developing fetal hippocampus and that substantial effects are evident for at least 2 weeks after sGC exposure.
AU - Crudo, Ariann
AU - Petropoulos, Sophie
AU - Suderman, Matthew
AU - Moisiadis, Vasilis G.
AU - Kostaki, Alisa
AU - Hallett, Michael
AU - Szyf, Moshe
AU - Matthews, Stephen G.
DA - 2013/11//
DO - 10.1210/en.2013-1484

IS - 11
PY - 2013
SP - 4170
EP - 4181
TI - Effects of antenatal synthetic glucocorticoid on glucocorticoid receptor binding, DNA methylation, and genome-wide mRNA levels in the fetal male hippocampus
T2 - Endocrinology
VL - 154
ER -
TY - JOUR
AB - Objective: To investigate if antenatal glucocorticoid treatment has an effect on hippocampal histology of the human preterm newborn. Patients and Methods: Included were consecutive neonates with a gestational age between 24 and 32 weeks, who were born between 1991 to 2009, who had died within 4 days after delivery and underwent brain autopsy. Excluded were neonates with congenital malformations and neonates treated postnatally with glucocorticoids. The brains were routinely fixed, samples of the hippocampus were stained with haematoxylin and eosin and sections were examined for presence or absence of large and small neurons in regions of the hippocampus. Additional staining with GFAP, neurofilament and vimentin was performed to evaluate gliosis and myelination. The proliferation marker Ki67 was used to evaluate neuronal proliferation. Staining with acid fuchsin-thionin was performed to evaluate ischemic damage. Results: The hippocampi of ten neonates who had been treated with antenatal glucocorticoids showed a lower density of large neurons ($p = 0.01$) and neurons irrespective of size ($p = 0.02$) as compared to eleven neonates who had not been treated with glucocorticoids. No difference was found in density of small neurons, in myelination, gliosis, proliferation or ischemic damage. Conclusion: We found a significantly lower density of neurons in the hippocampus of neonates after antenatal glucocorticoid treatment. Although the pathophysiological and clinical interpretations of these findings are not clear, they are consistent with those from experiments in mice and rhesus monkeys. © 2012 Tijsseling et al.
AU - Tijsseling, Deodata
AU - Wijnberger, Lia D.E.
AU - Derks, Jan B.
AU - van Velthoven, Cindy T.J.
AU - de Vries, Willem B.
AU - van Bel, Frank
AU - Nikkels, Peter G.J.
AU - Visser, Gerard H.A.
DA - 2012/3//
DO - 10.1371/journal.pone.0033369
IS - 3
PY - 2012
TI - Effects of antenatal glucocorticoid therapy on hippocampal histology of preterm infants
T2 - PLoS ONE
VL - 7
ER -
TY - JOUR
AB - Background: Glucocorticoids play a critical role in normative regulation of

fetal brain development. Exposure to excessive levels may have detrimental consequences and disrupt maturational processes. This may especially be true when synthetic glucocorticoids are administered during the fetal period, as they are to women in preterm labor. This study investigated the consequences for brain development and affective problems of fetal exposure to synthetic glucocorticoids. Methods: Brain development and affective problems were evaluated in 54 children (56% female), aged 6 to 10, who were full term at birth. Children were recruited into two groups: those with and without fetal exposure to synthetic glucocorticoids. Structural magnetic resonance imaging scans were acquired and cortical thickness was determined. Child affective problems were assessed using the Child Behavior Checklist. Results: Children in the fetal glucocorticoid exposure group showed significant and bilateral cortical thinning. The largest group differences were in the rostral anterior cingulate cortex (rACC). More than 30% of the rACC was thinner among children with fetal glucocorticoid exposure. Furthermore, children with more affective problems had a thinner left rACC. Conclusions: Fetal exposure to synthetic glucocorticoids has neurologic consequences that persist for at least 6 to 10 years. Children with fetal glucocorticoid exposure had a thinner cortex primarily in the rACC. Our data indicating that the rACC is associated with affective problems in conjunction with evidence that this region is involved in affective disorders raise the possibility that glucocorticoid-associated neurologic changes increase vulnerability to mental health problems. © 2013 Society of Biological Psychiatry.
AU - Davis, Elysia Poggi
AU - Sandman, Curt A.
AU - Buss, Claudia
AU - Wing, Deborah A.
AU - Head, Kevin
DA - 2013/11//
DO - 10.1016/j.biopsych.2013.03.009
IS - 9
KW - Development
KW - MRI
KW - fetal programming
KW - glucocorticoid
KW - prenatal
KW - stress
PY - 2013
SP - 647
EP - 655
TI - Fetal glucocorticoid exposure is associated with preadolescent brain development
T2 - Biological Psychiatry
VL - 74
ER -
TY - JOUR
AB - Importance: Maternal antenatal corticosteroid treatment is standard care to accelerate fetal maturation when birth before 34 weeks is imminent. Recently, expansion of the indications beyond 34 gestational weeks has been debated. However, data about long-term outcomes remain limited, especially among infants who after treatment exposure are born at term. Objective: To study if antenatal

corticosteroid treatment is associated with mental and behavioral disorders in children born at term (≥37 weeks 0 days' gestation) and preterm (<37 weeks 0 days' gestation) and if unmeasured familial confounding explains these associations. Design, Setting, and Participants: Population-based retrospective cohort study using nationwide registries of all singleton live births in Finland surviving until 1 year and a within-sibpair comparison among term siblings. Children were born between January 1, 2006, and December 31, 2017, and followed up until December 31, 2017. Exposures: Maternal antenatal corticosteroid treatment. Main Outcomes and Measures: Primary outcome was any childhood mental and behavioral disorder diagnosed in public specialized medical care settings. Results: Of the 674877 singleton children born in Finland during the study period, 670097 were eligible for analysis. The median length of follow-up was 5.8 (interquartile-range, 3.1-8.7) years. Of the 14868 (2.22%; 46.1% female) corticosteroid treatment-exposed children, 6730 (45.27%) were born at term and 8138 (54.74%) were born preterm; of the 655229 (97.78%; 48.9% female) nonexposed children, 634757 (96.88%) were born at term and 20472 (3.12%) were born preterm. Among the 241621 eligible term-born maternal sibpairs nested within this population, 4128 (1.71%) pairs were discordant for treatment exposure. Treatment exposure, compared with nonexposure, was significantly associated with higher risk of any mental and behavioral disorder in the entire cohort of children (12.01% vs 6.45%; absolute difference, 5.56% [95% CI, 5.04%-6.19%]; adjusted hazard ratio [HR], 1.33 [95% CI, 1.26-1.41]), in term-born children (8.89% vs 6.31%; absolute difference, 2.58% [95% CI, 1.92%-3.29%]; HR, 1.47 [95% CI, 1.36-1.69]), and when sibpairs discordant for treatment exposure were compared with sibpairs concordant for nonexposure (6.56% vs 4.17% for within-sibpair differences; absolute difference, 2.40% [95% CI, 1.67%-3.21%]; HR, 1.38 [95% CI, 1.21-1.58]). In preterm-born children, the cumulative incidence rate of any mental and behavioral disorder was also significantly higher for the treatment-exposed compared with the nonexposed children, but the HR was not significant (14.59% vs 10.71%; absolute difference, 3.38% [95% CI, 2.95%-4.87%]; HR, 1.00 [95% CI, 0.92-1.09]). Conclusions and Relevance: In this population-based cohort study, exposure to maternal antenatal corticosteroid treatment was significantly associated with mental and behavioral disorders in children. These findings may help inform decisions about maternal antenatal corticosteroid treatment.
AU - Räikkönen, Katri
AU - Gissler, Mika
AU - Kajantie, Eero
DA - 2020/5//
DO - 10.1001/jama.2020.3937
IS - 19
PB - American Medical Association
PY - 2020
SP - 1924
EP - 1933
TI - Associations between Maternal Antenatal Corticosteroid Treatment and Mental and Behavioral Disorders in Children
T2 - JAMA - Journal of the American Medical Association
VL - 323
ER -
TY - JOUR

AB - Objectives: To study the association between antenatal corticosteroids treatment and childhood mental disorders in infants born at different gestational ages, and to investigate the effect of different administration timing. Study design: This population-based cohort study used data from the Taiwan National Health Insurance Research Database. All singleton live births born between 2004 and 2010 were enrolled and followed up for at least 6 years. The primary outcome was any childhood mental disorder. Secondary outcomes included 7 specific subgroups of mental disorders. Results: A total of 1 163 443 singleton infants were included in the analysis, and 16 847 (1.45%) infants were exposed to antenatal corticosteroid treatment. Children exposed to antenatal corticosteroids were found to have a higher risk of developing childhood mental disorders in the entire cohort (hazard ratio [HR], 1.13; 95% CI, 1.08-1.18), the term group (HR, 1.11; 95% CI, 1.05-1.16), and the late-preterm group (HR, 1.15; 95% CI, 1.06-1.25). The administration of corticosteroids in the early stage of pregnancy (<28 weeks of gestation) significantly increased the risk of childhood mental disorders (HR, 1.22; 95% CI, 1.14-1.31). Conclusions: Exposure to antenatal corticosteroid treatment increases the cumulative risk of childhood mental disorders and attention deficit hyperactivity disorders, both in term and late preterm infants. The administration of corticosteroids in the early stage of pregnancy tends to increase the risk of mental disorders.
AU - Lin, Yi Hsuan
AU - Lin, Ching Heng
AU - Lin, Ming Chih
AU - Hsu, Ya Chi
AU - Hsu, Chung Ting
DA - 2023/2//
DO - 10.1016/j.jpeds.2022.09.050
KW - attention deficit hyperactivity disorders
KW - corticosteroid
KW - late preterm
KW - mental disorders
KW - preterm
PB - Elsevier Inc.
PY - 2023
SP - 245
EP - 251.e2
TI - Antenatal Corticosteroid Exposure is Associated with Childhood Mental Disorders in Late Preterm and Term Infants
T2 - Journal of Pediatrics
VL - 253
ER -
TY - JOUR
AB - Background: It has been well recognized that antenatal administration of dexamethasone to pregnant women at risk of preterm delivery may markedly accelerate fetal maturation and reduce the risk of adverse perinatal outcomes in their preterm infants, particularly for births before 34 weeks of gestation. Since 2015, antenatal corticosteroid administration has been extended beyond 34 weeks of gestation by clinical guidelines, as it might have beneficial effects on fetal maturation and perinatal outcomes. However, concerns regarding the potential influence of antenatal corticosteroid treatment on offspring neurodevelopment have

been raised. Objective: This study aimed to investigate whether maternal antenatal corticosteroid administration was associated with neurodevelopment in infants at 1 year of age. Study Design: In this prospective and longitudinal birth cohort study, women were followed up throughout gestation, and their infants underwent a Bayley Scales of Infant and Toddler Development, Third Edition, screening test at 1 year of age between December 2018 and September 2020. Finally, 1609 pregnant women and 1759 infants were included in the current study. Using a generalized linear mixed model, we examined the association between antenatal corticosteroid exposure and infant neurodevelopment in cognitive, receptive communication, expressive communication, fine motor, and gross motor functions. Results: Of the 1759 infants eligible for this study, 1453 (82.6%) were singletons. A total of 710 infants were exposed to antenatal corticosteroids, among whom 415 were dexamethasone exposed and 483 were prednisone exposed. Dexamethasone was prescribed most often in late pregnancy, whereas prednisone was often used before 8 weeks of gestation among women who conceived through assisted reproductive technology. Compared with those who had no exposure, antenatal corticosteroid exposure was associated with an increased risk of infants being noncompetent in the cognitive development domain after adjusting for conventional risk factors (adjusted risk ratio, 1.53; 95% confidence interval, 1.08–2.18; P=.017). For medication-specific exposure, those exposed vs not exposed to antenatal dexamethasone were 1.62-fold (95% confidence interval, 1.10–2.38; P=.014) more likely to be noncompetent in the cognitive development domain at 1 year. The association did not vary markedly between preterm and term infants, singletons and twins, or assisted reproductive technology–conceived and spontaneously conceived infants (all P>.05 for heterogeneity). In contrast, a null association was observed for the risk of being noncompetent in any domain of neurodevelopment with antenatal prednisone exposure at early pregnancy. Conclusion: Here, antenatal corticosteroid, particularly dexamethasone exposure, was markedly associated with an increased risk of infants being noncompetent in the cognitive development domain at 1 year of age. These findings may provide new information when weighing the benefits and potential risks of maternal antenatal corticosteroid administration.
AU - Tao, Shiyao
AU - Du, Jiangbo
AU - Chi, Xia
AU - Zhu, Yeyi
AU - Wang, Xiaoyan
AU - Meng, Qingxia
AU - Ling, Xiufeng
AU - Diao, Feiyang
AU - Song, Ci
AU - Jiang, Yangqian
AU - Lv, Hong
AU - Lu, Qun
AU - Qin, Rui
AU - Huang, Lei
AU - Xu, Xin
AU - Liu, Cong
AU - Ding, Yuqing
AU - Jiang, Tao
AU - Ma, Hongxia

AU - Xia, Yankai
AU - Liu, Jiayin
AU - Lin, Yuan
AU - Jin, Guangfu
AU - Hu, Zhibin
DA - 2022/11//
DO - 10.1016/j.ajog.2022.05.060
IS - 5
KW - 1 year old
KW - antenatal dexamethasone
KW - antenatal prednisone
KW - cognitive
KW - expressive communication
KW - fine motor
KW - gross motor
KW - intrauterine exposure
KW - receptive communication
PB - Elsevier Inc.
PY - 2022
SP - 759.e1
EP - 759.e15
TI - Associations between antenatal corticosteroid exposure and neurodevelopment in infants
T2 - American Journal of Obstetrics and Gynecology
VL - 227
ER -
TY - JOUR
AB - ImportanceA single course of antenatal corticosteroid therapy is recommended for pregnant women at risk of preterm birth between 24 and 33 weeks' gestational age. However, 50% of women remain pregnant 7 to 14 days later, leading to the question of whether additional courses should be given to women remaining at risk for preterm birth. The Multiple Courses of Antenatal Corticosteroids for Preterm Birth Study (MACS) was an international randomized clinical trial that compared multiple courses of antenatal corticosteroids with a single course in women at risk of preterm birth. OBJECTIVE To determine the effects of single vs multiple courses of antenatal corticosteroid therapy on death or neurodevelopmental disability (neuromotor, neurosensory, or neurocognitive/neurobehavioral function) at 5 years of age in children whose mothers participated in MACS. Our secondary aims were to determine the effect on height, weight, head circumference, blood pressure, intelligence, and specific cognitive (visual, spatial, and language) skills. DESIGN, SETTING, AND PARTICIPANTS Cohort follow-up study of children seen between June 2006 and May 2012 at 55 centers. In total, 1724 women (2141 children) were eligible for the study, of whom 1728 children (80.7%of the 2141 eligible children) participated and 1719 children contributed to the primary outcome. INTERVENTION Single and multiple courses of antenatal corticosteroid therapy. MAIN OUTCOMES AND MEASURES The primary outcomewas death or survival with a neurodevelopmental disability in 1 of the following domains: neuromotor (nonambulatory cerebral palsy), neurosensory (blindness, deafness, or need for visual/hearing aids), or neurocognitive/neurobehavioral function (abnormal attention, memory, or behavior). RESULTS There was no significant difference between the groups in the risk of death

or neurodevelopmental disability: 217 of 871 children (24.9%) in the multiple-courses group vs 210 of 848 children (24.8%) in the single-course group (odds ratio, 1.02 [95%CI, 0.81 to 1.29]; P = .84). CONCLUSIONS AND RELEVANCE Multiple courses, compared with a single course, of antenatal corticosteroid therapy did not increase or decrease the risk of death or disability at 5 years of age. Because of a lack of strong conclusive evidence of short-term or long-term benefits, it remains our opinion that multiple courses not be recommended in women with ongoing risk of preterm birth. TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT00187382 and International Standard Randomized Controlled Trial Number Register identifier ISRCTN2654148. Copyright 2013 American Medical Association.
AU - Asztalos, Elizabeth V.
AU - Murphy, Kellie E.
AU - Willan, Andrew R.
AU - Matthews, Stephen G.
AU - Ohlsson, Arne
AU - Saigal, Saroj
AU - Armson, B. Anthony
AU - Kelly, Edmond N.
AU - Delisle, Marie France
AU - Gafni, Amiram
AU - Lee, Shoo K.
AU - Sananes, Renee
AU - Rovet, Joanne
AU - Guselle, Patricia
AU - Amankwah, Kofi
AU - Saleem, Mariam
AU - Sanchez, Johanna
DA - 2013/12//
DO - 10.1001/jamapediatrics.2013.2764
IS - 12
PY - 2013
SP - 1102
EP - 1110
TI - Multiple courses of antenatal corticosteroids for preterm Birth study outcomes in children at 5 years of age (MACS-5)
T2 - JAMA Pediatrics
VL - 167
ER -
TY - RPRT
AU - Wapner, Ronald J
AU - Sorokin, Yoram
AU - Mele, Lisa
AU - Johnson, Francee
AU - Dudley, Donald J
AU - Spong, Catherine Y
AU - Peaceman, Alan M
AU - Leveno, Kenneth J
AU - Malone, Fergal
AU - Caritis, Steve N

AU - Mercer, Brian
AU - Harper, Margaret
AU - Rouse, Dwight J
AU - Thorp, John M
AU - Ramin, Susan
AU - Carpenter, Marshall W
AU - Gabbe, Steven G
PY - 2007
SP - 1190
EP - 1198
TI - Long-Term Outcomes after Repeat Doses of Antenatal Corticosteroids A bs t r ac t
T2 - N Engl J Med
UR - www.nejm.org
VL - 357
ER -
TY - JOUR
AB - To determine whether antenatal betamethasone prior to elective term caesarean section (CS) affects long term behavioural, cognitive or developmental outcome, and whether the risk of asthma or atopic disease is reduced. A questionnaire based follow-up of a multicentre randomised controlled trial (Antenatal Steroids for Term Elective Caesarean Section, BMJ 2005). Four UK study centres from the original trial. 862 participants from the four largest recruiting centres, 92% of the original study. 824 (96%) were traced and 799 (93%) were successfully contacted. Fifty-one percent (407/799) completed and returned the questionnaire. The children were aged 8-15 years (median 12.2 years, 52% girls). 386 gave consent to contact schools with 352 (91%) reports received. Questionnaires including a strengths and difficulties questionnaire, International Study of Asthma and Allergies in Childhood, general health and school performance. There were no significant differences between children whose mothers received betamethasone and controls for the mean total strengths and difficulties questionnaire scores and subscores for hyperactivity, emotional symptoms, prosocial behaviour, conduct or peer problems. 25 (12%) children whose mothers received betamethasone had reported learning difficulties compared with 27 (14%) control children. The proportion of children who achieved standard assessment tests KS2 exams level 4 or above for mathematics, English or science was similar as were the rates of ever reported wheeze (30% vs 30%), asthma (24% vs 21%), eczema (34% vs 37%) and hay fever (25% vs 27%). Antenatal betamethasone did not result in any adverse outcomes or reduction in asthma or atopy. It should be considered for elective CS at 37-38 weeks of gestation. : Original trial was preregistration, the trial publication is BMJ. 2005 Sep 24;331(7518):662.
AU - Stutchfield, Peter Roy
AU - Whitaker, Rhiannon
AU - Gliddon, Angela E.
AU - Hobson, Lucie
AU - Kotecha, Sailesh
AU - Doull, Iolo J.M.
DO - 10.1136/archdischild-2012-303157
IS - 3
PY - 2013

TI - Behavioural, educational and respiratory outcomes of antenatal betamethasone for term caesarean section (ASTECS trial).
T2 - Archives of disease in childhood. Fetal and neonatal edition
VL - 98
ER -
TY - GEN
AB - Background: Systematic reviews have been considered as the pillar on which evidence-based healthcare rests. Systematic review methodology has evolved and been modified over the years to accommodate the range of questions that may arise in the health and medical sciences. This paper explores a concept still rarely considered by novice authors and in the literature: determining the type of systematic review to undertake based on a research question or priority. Results: Within the framework of the evidence-based healthcare paradigm, defining the question and type of systematic review to conduct is a pivotal first step that will guide the rest of the process and has the potential to impact on other aspects of the evidence-based healthcare cycle (evidence generation, transfer and implementation). It is something that novice reviewers (and others not familiar with the range of review types available) need to take account of but frequently overlook. Our aim is to provide a typology of review types and describe key elements that need to be addressed during question development for each type. Conclusions: In this paper a typology is proposed of various systematic review methodologies. The review types are defined and situated with regard to establishing corresponding questions and inclusion criteria. The ultimate objective is to provide clarified guidance for both novice and experienced reviewers and a unified typology with respect to review types.
AU - Munn, Zachary
AU - Stern, Cindy
AU - Aromataris, Edoardo
AU - Lockwood, Craig
AU - Jordan, Zoe
DA - 2018/1//
DO - 10.1186/s12874-017-0468-4
IS - 1
KW - Evidence-based healthcare
KW - Question development
KW - Systematic reviews
PB - BioMed Central Ltd.
PY - 2018
TI - What kind of systematic review should i conduct? A proposed typology and guidance for systematic reviewers in the medical and health sciences
T2 - BMC Medical Research Methodology
VL - 18
ER -
TY - GEN
AU - Health Sciences Library System
PY - 2024
TI - Systematic, scoping, and similar reviews and meta-analyses - PubMed Search Filters - LibGuides at Health Sciences Library System
UR -
https://hsls.libguides.com/PubMed-search-filters/systematic-reviews#SR-MA-combined

ER -
TY - GEN
AB - Fractional anisotropy (FA), axial diffusivity (AD), and radial diffusivity (RD) are commonly used as MRI biomarkers of white matter microstructure in diffusion MRI studies of neurodevelopment, brain aging, and neurologic injury/disease. Some of the more frequent practices include performing voxel-wise or region-based analyses of these measures to cross-sectionally compare individuals or groups, longitudinally assess individuals or groups, and/or correlate with demographic, behavioral or clinical variables. However, it is now widely recognized that the majority of cerebral white matter voxels contain multiple fiber populations with different trajectories, which renders these metrics highly sensitive to the relative volume fractions of the various fiber populations, the microstructural integrity of each constituent fiber population, and the interaction between these factors. Many diffusion imaging experts are aware of these limitations and now generally avoid using FA, AD or RD (at least in isolation) to draw strong reverse inferences about white matter microstructure, but based on the continued application and interpretation of these metrics in the broader biomedical/neuroscience literature, it appears that this has perhaps not yet become common knowledge among diffusion imaging end-users. Therefore, this paper will briefly discuss the complex biophysical underpinnings of these measures in the context of crossing fibers, provide some intuitive “thought experiments” to highlight how conventional interpretations can lead to incorrect conclusions, and suggest that future studies refrain from using (over-interpreting) FA, AD, and RD values as standalone biomarkers of cerebral white matter microstructure.
AU - Figley, Chase R.
AU - Uddin, Md Nasir
AU - Wong, Kaihim
AU - Kornelsen, Jennifer
AU - Puig, Josep
AU - Figley, Teresa D.
DA - 2022/1//
DO - 10.3389/fnins.2021.799576
KW - axial diffusivity
KW - crossing fibers
KW - diffusion MRI
KW - fractional anisotropy
KW - radial diffusivity
KW - white matter
PB - Frontiers Media S.A.
PY - 2022
TI - Potential Pitfalls of Using Fractional Anisotropy, Axial Diffusivity, and Radial Diffusivity as Biomarkers of Cerebral White Matter Microstructure
T2 - Frontiers in Neuroscience
VL - 15
ER -
TY - JOUR
AB - Background: The assessment of multiple systematic reviews (AMSTAR) tool is widely used for investigating the methodological quality of systematic reviews (SR). Originally, AMSTAR was developed for SRs of randomized controlled trials (RCTs). Its applicability to SRs of other study designs remains unclear. Our

objectives were to: 1) analyze how AMSTAR is applied by authors and (2) analyze whether the authors pay attention to the original purpose of AMSTAR and for what it has been validated. Methods: We searched MEDLINE (via PubMed) from inception through October 2016 to identify studies that applied AMSTAR. Full-text studies were sought for all retrieved hits and screened by one reviewer. A second reviewer verified the excluded studies (liberal acceleration). Data were extracted into structured tables by one reviewer and were checked by a second reviewer. Discrepancies at any stage were resolved by consensus or by consulting a third person. We analyzed the data descriptively as frequencies or medians and interquartile ranges (IQRs). Associations were quantified using the risk ratio (RR), with 95% confidence intervals. Results: We identified 247 studies. They included a median of 17 reviews (interquartile range (IQR): 8 to 47) per study. AMSTAR was modified in 23% (57/247) of studies. In most studies, an AMSTAR score was calculated (200/247; 81%). Methods for calculating an AMSTAR score varied, with summing up all yes answers (yes = 1) being the most frequent option (102/200; 51%). More than one third of the authors failed to report how the AMSTAR score was obtained (71/200; 36%). In a subgroup analysis, we compared overviews of reviews (n = 154) with the methodological publications (n = 93). The overviews of reviews were much less likely to mention both limitations with respect to study designs (if other studies other than RCTs were included in the reviews) (RR 0.27, 95% CI 0.09 to 0.75) and overall score (RR 0.08, 95% CI 0.02 to 0.35). Conclusions: Authors, peer reviewers, and editors should pay more attention to the correct use and reporting of assessment tools in evidence synthesis. Authors of overviews of reviews should ensure to have a methodological expert in their review team.
AU - Pieper, Dawid
AU - Koensgen, Nadja
AU - Breuing, Jessica
AU - Ge, Long
AU - Wegewitz, Uta
DA - 2018/6//
DO - 10.1186/s12874-018-0520-z
IS - 1
KW - AMSTAR
KW - Methodological study
KW - Quality assessment
KW - Reporting
KW - Systematic review
PB - BioMed Central Ltd.
PY - 2018
TI - How is AMSTAR applied by authors - A call for better reporting
T2 - BMC Medical Research Methodology
VL - 18
ER -
TY - JOUR
AB - Overlap of primary studies among systematic reviews (SRs) is one of the main methodological challenges when conducting overviews. If not assessed properly, overlapped primary studies may mislead findings, since they may have a major influence either in qualitative analyses or in statistical weight. Moreover, overlapping SRs may represent the existence of duplicated efforts. Matrices of evidence and the calculation of the overall corrected covered area (CCA) are

appropriate methods to address this issue, but they seem to be not comprehensive enough. In this article we present Graphical Representation of Overlap for OVErviews (GROOVE), an easy-to-use tool for overview authors. Starting from a matrix of evidence, GROOVE provides the number of included primary studies and SRs included in the matrix; the absolute number of overlapped and non-overlapped primary studies; and an overall CCA assessment. The tool also provides a detailed CCA assessment for each possible pair of SRs (or “nodes”), with a graphical and easy-to-read representation of these results. Additionally, it includes an advanced optional usage, incorporating structural missingness in the matrix. In this article, we show the details about how to use GROOVE, what results it achieves and how the tool obtains these results. GROOVE is intended to improve the overlap assessment by making it easier, faster, and more friendly for both authors and readers. The tool is freely available at http://doi.org/10.17605/OSF.IO/U2MS4 and https://es.cochrane.org/es/groovetool.
AU - Pérez-Bracchiglione, Javier
AU - Meza, Nicolás
AU - Bangdiwala, Shrikant I.
AU - Niño de Guzmán, Ena
AU - Urrútia, Gerard
AU - Bonfill, Xavier
AU - Madrid, Eva
DA - 2022/5//
DO - 10.1002/jrsm.1557
IS - 3
KW - corrected covered area
KW - overlap
KW - overviews of systematic reviews
KW - systematic reviews as topic
PB - John Wiley and Sons Ltd
PY - 2022
SP - 381
EP - 388
TI - Graphical Representation of Overlap for OVErviews: GROOVE tool
T2 - Research Synthesis Methods
VL - 13
ER -
TY - JOUR
AB - Background: Reporting standards, such as PRISMA aim to ensure that the methods and results of systematic reviews are described in sufficient detail to allow full transparency. Flow diagrams in evidence syntheses allow the reader to rapidly understand the core procedures used in a review and examine the attrition of irrelevant records throughout the review process. Recent research suggests that use of flow diagrams in systematic reviews is poor and of low quality and called for standardised templates to facilitate better reporting in flow diagrams. The increasing options for interactivity provided by the Internet gives us an opportunity to support easy-to-use evidence synthesis tools, and here we report on the development of a tool for the production of PRISMA 2020-compliant systematic review flow diagrams. Methods and Findings: We developed a free-to-use, Open Source R package and web-based Shiny app to allow users to design PRISMA flow diagrams for their own systematic reviews. Our tool allows users to produce standardised

visualisations that transparently document the methods and results of a systematic review process in a variety of formats. In addition, we provide the opportunity to produce interactive, web-based flow diagrams (exported as HTML files), that allow readers to click on boxes of the diagram and navigate to further details on methods, results or data files. We provide an interactive example here; https://prisma-flowdiagram.github.io/. Conclusions: We have developed a user-friendly tool for producing PRISMA 2020-compliant flow diagrams for users with coding experience and, importantly, for users without prior experience in coding by making use of Shiny (https://estech.shinyapps.io/prisma_flowdiagram/). This free-to-use tool will make it easier to produce clear and PRISMA 2020-compliant systematic review flow diagrams. Significantly, users can also produce interactive flow diagrams for the first time, allowing readers of their reviews to smoothly and swiftly explore and navigate to further details of the methods and results of a review. We believe this tool will increase use of PRISMA flow diagrams, improve the compliance and quality of flow diagrams, and facilitate strong science communication of the methods and results of systematic reviews by making use of interactivity. We encourage the systematic review community to make use of the tool, and provide feedback to streamline and improve their usability and efficiency.
AU - Haddaway, Neal R.
AU - Page, Matthew J.
AU - Pritchard, Chris C.
AU - McGuinness, Luke A.
DA - 2022/6//
DO - 10.1002/cl2.1230
IS - 2
PB - John Wiley and Sons Inc
PY - 2022
TI - PRISMA2020: An R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital transparency and Open Synthesis
T2 - Campbell Systematic Reviews
VL - 18
ER -
TY - GEN
AB - Background: Respiratory morbidity including respiratory distress syndrome (RDS) is a serious complication of preterm birth and the primary cause of early neonatal mortality and disability. While researching the effects of the steroid dexamethasone on premature parturition in fetal sheep in 1969, Liggins found that there was some inflation of the lungs of lambs born at gestations at which the lungs would be expected to be airless. Liggins and Howie published the first randomised controlled trial in humans in 1972 and many others followed. Objectives: To assess the effects of administering a course of corticosteroids to the mother prior to anticipated preterm birth on fetal and neonatal morbidity and mortality, maternal mortality and morbidity, and on the child in later life. Search methods: We searched Cochrane Pregnancy and Childbirth's Trials Register (17 February 2016) and reference lists of retrieved studies. Selection criteria: We considered all randomised controlled comparisons of antenatal corticosteroid administration (betamethasone, dexamethasone, or hydrocortisone) with placebo, or with no treatment, given to women with a singleton or multiple pregnancy, prior to

anticipated preterm delivery (elective, or following spontaneous labour), regardless of other co-morbidity, for inclusion in this review. Most women in this review received a single course of steroids; however, nine of the included trials allowed for women to have weekly repeats. Data collection and analysis: Two review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy. The quality of the evidence was assessed using the GRADE approach. Main results: This update includes 30 studies (7774 women and 8158 infants). Most studies are of low or unclear risk for most bias domains. An assessment of high risk usually meant a trial had potential for performance bias due to lack of blinding. Two trials had low risks of bias for all risk of bias domains. Treatment with antenatal corticosteroids (compared with placebo or no treatment) is associated with a reduction in the most serious adverse outcomes related to prematurity, including: perinatal death (average risk ratio (RR) 0.72, 95% confidence interval (CI) 0.58 to 0.89; participants = 6729; studies = 15; Tau2 = 0.05, I2 = 34%; moderate-quality); neonatal death (RR 0.69, 95% CI 0.59 to 0.81; participants = 7188; studies = 22), RDS (average RR 0.66, 95% CI 0.56 to 0.77; participants = 7764; studies = 28; Tau2 = 0.06, I2 = 48%; moderate-quality); moderate/severe RDS (average RR 0.59, 95% CI 0.38 to 0.91; participants = 1686; studies = 6; Tau2 = 0.14, I2 = 52%); intraventricular haemorrhage (IVH) (average RR 0.55, 95% CI 0.40 to 0.76; participants = 6093; studies = 16; Tau2 = 0.10, I2 = 33%; moderate-quality), necrotising enterocolitis (RR 0.50, 95% CI 0.32 to 0.78; participants = 4702; studies = 10); need for mechanical ventilation (RR 0.68, 95% CI 0.56 to 0.84; participants = 1368; studies = 9); and systemic infections in the first 48 hours of life (RR 0.60, 95% CI 0.41 to 0.88; participants = 1753; studies = 8). There was no obvious benefit for: chronic lung disease (average RR 0.86, 95% CI 0.42 to 1.79; participants = 818; studies = 6; Tau2 = 0.38 I2 = 65%); mean birthweight (g) (MD -18.47, 95% CI -40.83 to 3.90; participants = 6182; studies = 16; moderate-quality); death in childhood (RR 0.68, 95% CI 0.36 to 1.27; participants = 1010; studies = 4); neurodevelopment delay in childhood (RR 0.64, 95% CI 0.14 to 2.98; participants = 82; studies = 1); or death into adulthood (RR 1.00, 95% CI 0.56 to 1.81; participants = 988; studies = 1). Treatment with antenatal corticosteroids does not increase the risk of chorioamnionitis (RR 0.83, 95% CI 0.66 to 1.06; participants = 5546; studies = 15; moderate-quality evidence) or endometritis (RR 1.20, 95% CI 0.87 to 1.63; participants = 4030; studies = 10; Tau2 = 0.11, I2 = 28%; moderate-quality). No increased risk in maternal death was observed. However, the data on maternal death is based on data from a single trial with two deaths; four other trials reporting maternal death had zero events (participants = 3392; studies = 5; moderate-quality). There is no definitive evidence to suggest that antenatal corticosteroids work differently in any pre-specified subgroups (singleton versus multiple pregnancy; membrane status; presence of hypertension) or for different study protocols (type of corticosteroid; single course or weekly repeats). GRADE outcomes were downgraded to moderate-quality. Downgrading decisions (for perinatal death, RDS, IVH, and mean birthweight) were due to limitations in study design or concerns regarding precision (chorioamnionitis, endometritis). Maternal death was downgraded for imprecision due to few events. Authors' conclusions: Evidence from this update supports the continued use of a single course of antenatal corticosteroids to accelerate fetal lung maturation in women at risk of preterm birth. A single course of antenatal corticosteroids could be considered routine for preterm delivery. It is important to note that most of the evidence comes from high income countries and

hospital settings; therefore, the results may not be applicable to low-resource settings with high rates of infections. There is little need for further trials of a single course of antenatal corticosteroids versus placebo in singleton pregnancies in higher income countries and hospital settings. However, data are sparse in lower income settings. There are also few data regarding risks and benefits of antenatal corticosteroids in multiple pregnancies and other high-risk obstetric groups. Further information is also required concerning the optimal dose-to-delivery interval, and the optimal corticosteroid to use. We encourage authors of previous studies to provide further information, which may answer any remaining questions about the use of antenatal corticosteroids in such pregnancies without the need for further randomised controlled trials. Individual patient data meta-analysis from published trials is likely to answer some of the evidence gaps. Follow-up studies into childhood and adulthood, particularly in the late preterm gestation and repeat courses groups, are needed. We have not examined the possible harmful effects of antenatal corticosteroids in low-resource settings in this review. It would be particularly relevant to explore this finding in adequately powered prospective trials.
AU - Roberts, Devender
AU - Brown, Julie
AU - Medley, Nancy
AU - Dalziel, Stuart R.
DA - 2017/3//
DO - 10.1002/14651858.CD004454.pub3
IS - 3
PB - John Wiley and Sons Ltd
PY - 2017
TI - Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth
T2 - Cochrane Database of Systematic Reviews
VL - 2017
ER -
TY - GEN
AB - Objective: To systematically review and integrate data on the neurodevelopmental outcome of children after administration of a single course of antenatal corticosteroids for threatened preterm labor. DATA SOURCES: MEDLINE, Scopus, CENTRAL, and www.clinicaltrials.gov (inception to August 2014) using combinations of the terms "prenatal," "antenatal," "cortico," "steroid," "betamethasone," "dexamethasone," "neurodevelopment," "development," and "follow-up." We perused the references of the retrieved articles. METHODS OF STUDY SELECTION: We included randomized and nonrandomized trials reporting on the neurodevelopmental outcomes of children whose mothers were administered a single course of betamethasone or dexamethasone antenatally for threatened preterm birth as opposed to placebo or no treatment. TABULATION, INTEGRATION, AND Results: Summary risk ratio (RR) was calculated for dichotomous data; standardized mean difference was calculated for trials that measured the same outcome but used different methods. Heterogeneity was assessed using the I 2 statistic. Sensitivity and subgroup analyses were planned according to study design, specific steroid, and mean gestational age at birth. A single course of antenatal corticosteroids was associated with reduced risk for cerebral palsy (seven studies; treated: 390 of 5,199, untreated: 146 of 1,379; RR 0.678, 95% confidence interval [CI]

0.564-0.815), psychomotor development index less than 70 (two studies; treated: 783 of 3,049, untreated: 258 of 969; RR 0.829, 95% CI 0.737-0.933), and severe disability (five studies; treated: 1,567 of 4,840, untreated: 475 of 1,211; RR 0.787, 95% CI 0.729-0.850). Steroid treatment increased the rates of intact survival (six studies; treated: 1,082 of 2,013, untreated: 273 of 561; RR 1.186, 95% CI 1.056-1.332). Betamethasone was found to significantly decrease the risk for severe disability and increase the rate of intact survival. Dexamethasone increased the rate of intact survival; however, data for dexametasone and the other planned subgroup analyses were limited (fewer than 1,000 children at most). The major limitations involved inclusion of nonrandomized studies and scarcity of data on finer neurodevelopmental outcomes. Conclusion: A single course of antenatal corticosteroids in women at high risk for preterm birth appears to improve most neurodevelopmental outcomes in offspring born before 34 weeks of gestation.
AU - Sotiriadis, Alexandros
AU - Tsiami, Alexandra
AU - Papatheodorou, Stefania
AU - Baschat, Ahmet A.
AU - Sarafidis, Kosmas
AU - Makrydimas, George
DA - 2015/6//
DO - 10.1097/AOG.0000000000000748
IS - 6
PB - Lippincott Williams and Wilkins
PY - 2015
SP - 1385
EP - 1396
TI - Neurodevelopmental outcome after a single course of antenatal steroids in children born preterm: A systematic review and meta-analysis
T2 - Obstetrics and Gynecology
VL - 125
ER -
TY - GEN
AB - Objective. To systematically review the efficacy and safety of repeated antenatal corticosteroid on neonatal morbidity, growth and later development. Design. MEDLINE, Cochrane database and a bibliography of identified articles were searched for English language studies. Design.Meta-analysis of randomized controlled trials. Sample. Randomized, controlled trials studying the efficacy and safety of repeat antenatal corticosteroid treatment on neonatal morbidity and early childhood development. Main outcome measures. Respiratory distress syndrome, intrauterine growth, neurodevelopment. Methods. Two reviewers independently assessed titles, abstracts and full studies, extracted data and assessed quality. Meta-analyses were performed, calculating risk ratios and weighted differences of means with 95% confidence intervals using a random-effects model. Results. Eight trials were included. Repeated betamethasone treatment decreased the risk of respiratory distress syndrome (relative risk 0.85, 95% confidence interval 0.77-0.93). Trials involving weekly or biweekly repeated betamethasone and those involving a single rescue dose decreased the risk of respiratory distress syndrome. Intrauterine growth was significantly restricted among preterm infants exposed to weekly or biweekly repeated betamethasone. A single rescue course did not affect growth. Four follow-up studies did not reveal any disturbances in neurodevelopment

or growth at two years of corrected age. Conclusions. Repeated corticosteroid treatment decreased the risk of respiratory distress syndrome among preterm infants. Weekly or biweekly repeated betamethasone restricted intrauterine growth, which raises concerns about long-term consequences on neurodevelopment and metabolism. More follow-up studies are needed to confirm the long-term safety of repeated betamethasone. © 2011 The Authors Acta Obstetricia et Gynecologica Scandinavica © 2011 Nordic Federation of Societies of Obstetrics and Gynecology.
AU - Peltoniemi, Outi M.
AU - Kari, M. Anneli
AU - Hallman, Mikko
DA - 2011/7//
DO - 10.1111/j.1600-0412.2011.01132.x
IS - 7
KW - Antenatal period
KW - Betamethasone
KW - Corticosteroid
KW - Meta-analysis
KW - Prematurity
PY - 2011
SP - 719
EP - 727
TI - Repeated antenatal corticosteroid treatment: A systematic review and meta-analysis
T2 - Acta Obstetricia et Gynecologica Scandinavica
VL - 90
ER -
TY - GEN
AB - Background: It has been unclear whether repeat dose(s) of prenatal corticosteroids are beneficial. Objectives: To assess the effectiveness and safety of repeat dose(s) of prenatal corticosteroids. Search methods: We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (20 January 2015), searched reference lists of retrieved studies and contacted authors for further data. Selection criteria: Randomised controlled trials of women who had already received a single course of corticosteroids seven or more days previously and considered still at risk of preterm birth. Data collection and analysis: We assessed trial quality and extracted data independently. Main results: We included 10 trials (a total of 4733 women and 5700 babies) with low to moderate risk of bias. Treatment of women who remain at risk of preterm birth seven or more days after an initial course of prenatal corticosteroids with repeat dose(s), compared with no repeat corticosteroid treatment, reduced the risk of their infants experiencing the primary outcomes respiratory distress syndrome (risk ratio (RR) 0.83, 95% confidence interval (CI) 0.75 to 0.91, eight trials, 3206 infants, number needed to treat to benefit (NNTB) 17, 95% CI 11 to 32) and serious infant outcome (RR 0.84, 95% CI 0.75 to 0.94, seven trials, 5094 infants, NNTB 30, 95% CI 19 to 79). Treatment with repeat dose(s) of corticosteroid was associated with a reduction in mean birthweight (mean difference (MD) -75.79 g, 95% CI -117.63 to -33.96, nine trials, 5626 infants). However, outcomes that adjusted birthweight for gestational age (birthweight Z scores, birthweight multiples of the median and small-for-gestational age) did not differ between treatment groups. At early childhood follow-up, no statistically significant differences were seen for infants

exposed to repeat prenatal corticosteroids compared with unexposed infants for the primary outcomes (total deaths; survival free of any disability or major disability; disability; or serious outcome) or in the secondary outcome growth assessments. In women, for the two primary outcomes, there was no increase in infectious morbidity of chorioamnionitis or puerperal sepsis, and the likelihood of a caesarean birth was unchanged. Authors' conclusions: The short-term benefits for babies of less respiratory distress and fewer serious health problems in the first few weeks after birth support the use of repeat dose(s) of prenatal corticosteroids for women still at risk of preterm birth seven days or more after an initial course. These benefits were associated with a small reduction in size at birth. The current available evidence reassuringly shows no significant harm in early childhood, although no benefit. Further research is needed on the long-term benefits and risks for the woman and baby. Individual patient data meta-analysis may clarify how to maximise benefit and minimise harm.
AU - Crowther, Caroline A.
AU - Mckinlay, Christopher J.D.
AU - Middleton, Philippa
AU - Harding, Jane E.
DA - 2015/7//
DO - 10.1002/14651858.CD003935.pub4
IS - 7
PB - John Wiley and Sons Ltd
PY - 2015
TI - Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes
T2 - Cochrane Database of Systematic Reviews
VL - 2015
ER -
TY - GEN
AB - Multiple courses versus a single course of antenatal corticosteroids (ACS) have been associated with mild respiratory benefits but also adverse outcomes like smaller head circumference and birth weight. Long-term effects warrant study. We systematically reviewed long-term outcomes (≥1 year) in both preterm and term birth after exposure to preterm multiple courses (including a rescue dose or course) versus a single course. We searched seven databases from January 2000 to October 2021. We included follow-up studies of randomized controlled trials (RCTs) and cohort studies with births occurring in/after the year 2000, given advances in perinatal care. Two reviewers assessed titles/abstracts, articles, quality, and outcomes including psychological disorders, neurodevelopment, and anthropometry. Six follow-up studies of three RCTs and two cohort studies (over 2,860 children total) met inclusion criteria. Among children born preterm, randomization to multiple courses versus a single course of ACS was not associated with adjusted beneficial or adverse neurodevelopmental/psychological or other outcomes, but data are scant after a rescue dose (120 and 139 children, respectively, low certainty) and nonexistent after a rescue course. For children born at term (i.e., 27% of the multiple courses of ACS 5-year follow-up study of 1,728 preterm/term born children), preterm randomization to multiple courses (at least one additional course) versus a single course was significantly associated with elevated odds of neurosensory impairment (adjusted odds ratio = 3.70, 95% confidence interval: 1.57-8.75; 212 and 247 children, respectively, moderate certainty). In this

systematic review of long-term outcomes after multiple courses versus a single course of ACS, there were no significant benefits or risks regarding neurodevelopment in children born preterm but little data after one rescue dose and none after a rescue course. However, multiple courses (i.e., at least one additional course) should be considered cautiously: after term birth, there are no long-term benefits but neurosensory harms. Key Points We systematically reviewed the long-term impact of multiple versus a single course of ACS. Long-term follow-up data were scant after a rescue dose and absent after one rescue course of ACS. In children born preterm, multiple courses of ACS were not associated with long-term benefits/harms. In children born at term, multiple courses of ACS were associated with neurosensory impairment. Preterm administration of multiple courses of ACS should be considered cautiously.
AU - Ninan, Kiran
AU - Liyanage, Sugee K.
AU - Murphy, Kellie E.
AU - Asztalos, Elizabeth V.
AU - McDonald, Sarah D.
DA - 2024/3//
DO - 10.1055/s-0042-1760386
IS - 4
KW - antenatal corticosteroids
KW - long-term outcomes
KW - neurodevelopment
KW - systematic review
PB - Thieme Medical Publishers, Inc.
PY - 2024
SP - 395
EP - 404
TI - Long-Term Outcomes of Multiple versus a Single Course of Antenatal Steroids: A Systematic Review
T2 - American Journal of Perinatology
VL - 41
ER -
TY - GEN
AU - Ahlbom, Anders
DA - 2021/8//
DO - 10.1007/s10654-021-00778-w
IS - 8
PB - NLM (Medline)
PY - 2021
SP - 767
EP - 768
TI - Modern Epidemiology, 4th edition. TL Lash, TJ VanderWeele, S Haneuse, KJ Rothman. Wolters Kluwer, 2021
T2 - European journal of epidemiology
VL - 36
ER -
TY - JOUR
AU - Liauw, Jessica
AU - Campbell, Kayleigh S.J.

AU - Foggin, Hannah
AU - Grunau, Ruth E.
AU - Petrie, Julie
AU - Qasim, Anila
AU - Brignardello-Petersen, Romina
AU - Mishaal, Ram A.
AU - Hutcheon, Jennifer A.
DA - 2025/6//
DO - 10.1097/AOG.0000000000005950
PY - 2025
TI - Antenatal Corticosteroids and Child Neurodevelopment
T2 - Obstetrics & Gynecology
UR - https://journals.lww.com/10.1097/AOG.0000000000005950
ER -
TY - GEN
AB - Glucocorticoids (GCs) regulate distinct physiological processes in the developing fetus, in particular accelerating organ maturation that enables the fetus to survive outside the womb. In preterm birth, the developing fetus does not receive sufficient exposure to endogenous GCs in utero for proper organ development predisposing the neonate to complications including intraventricular hemorrhage, respiratory distress syndrome (RDS) and necrotizing enterocolitis (NEC). Synthetic GCs (sGCs) have proven useful in the prevention of these complications since they are able to promote the rapid maturation of underdeveloped organs present in the fetus. While these drugs have proven to be clinically effective in the prevention of IVH, RDS and NEC, they may also trigger adverse developmental side effects. This review will examine the current clinical use of antenatal sGC therapy in preterm birth, their placental metabolism, and their effects on the developing brain.
AU - Carson, Ross
AU - Monaghan-Nichols, A. Paula
AU - DeFranco, Donald B.
AU - Rudine, Anthony C.
DO - 10.1016/j.steroids.2016.05.012
KW - Antenatal
KW - Glucocorticoids
KW - Neurodevelopment
KW - Preterm birth
PB - Elsevier Inc.
PY - 2016
SP - 25
EP - 32
TI - Effects of antenatal glucocorticoids on the developing brain
T2 - Steroids
VL - 114
ER -
TY - JOUR
AB - The administration of antenatal corticosteroids has been widely adopted as the standard of care in the management of pregnancies at risk for preterm delivery before 37 weeks of gestation, with the primary goal of reducing neonatal morbidity. However, the long-term risks associated with antenatal corticosteroid use remain uncertain. The purpose of this Consult is to review the current literature on the

benefits and risks of antenatal corticosteroid use in the late preterm period and to provide recommendations based on the available evidence. The recommendations by the Society for Maternal-Fetal Medicine are as follows: (1) we recommend offering a single course of antenatal corticosteroids (2 doses of 12 mg of intramuscular betamethasone 24 hours apart) to patients who meet the inclusion criteria of the Antenatal Late Preterm Steroids trial, ie, those with a singleton pregnancy between 34 0/7 and 36 6/7 weeks of gestation who are at high risk of preterm birth within the next 7 days and before 37 weeks of gestation (GRADE 1A); (2) we suggest consideration for the use of antenatal corticosteroids in select populations not included in the original Antenatal Late Preterm Steroids trial, such as patients with multiple gestations reduced to a singleton gestation on or after 14 0/7 weeks of gestation, patients with fetal anomalies, or those who are expected to deliver in <12 hours (GRADE 2C); (3) we recommend against the use of antenatal corticosteroids for fetal lung maturity in pregnant patients with a low likelihood of delivery before 37 weeks of gestation (GRADE 1B); (4) we recommend against the use of late preterm corticosteroids in pregnant patients with pregestational diabetes mellitus, given the risk of worsening neonatal hypoglycemia (GRADE 1C); (5) we recommend that patients at risk for late preterm delivery be thoroughly counseled regarding the potential risks and benefits of antenatal corticosteroid administration and be advised that the long-term risks remain uncertain (GRADE 1C).
AU - Reddy, Uma M.
AU - Deshmukh, Uma
AU - Dude, Annie
AU - Harper, Lorie
AU - Osmundson, Sarah S.
DA - 2021/11//
DO - 10.1016/j.ajog.2021.07.023
IS - 5
KW - antenatal corticosteroids
KW - betamethasone
KW - fetal lung maturity
KW - preterm birth
PB - Elsevier Inc.
PY - 2021
SP - B36
EP - B42
TI - Society for Maternal-Fetal Medicine Consult Series #58: Use of antenatal corticosteroids for individuals at risk for late preterm delivery: Replaces SMFM Statement #4, Implementation of the use of antenatal corticosteroids in the late preterm birth period in women at risk for preterm delivery, August 2016
T2 - American Journal of Obstetrics and Gynecology
VL - 225
ER -
TY - JOUR
AB - study of the effect of antenatal dexamethasone on growth and development of premature children at the corrected age of 2 years. The objective of the series was to study the effect of prenatal dexamethasone therapy on the growth and neurological development of pretenn children until the age of 2 years. Eighty-two children with a mean gestational age of 30 (24-33) weeks and a mean weight of 1291 (530-236O)g at birth, treated antenatally with either dexamethasone (n = 50) or

placebo (n = 32). were examined at the adjusted age of 24 months by a paediatric neurologist, a neuropsychologist and a speech therapist. Neurological development was defined as normal if all scores of neuropaediatric, neuropsychological and verbal tests were within the normal range. Normal neurological development was found in 52% of the dexamethasone-treated and in 34% of the placebo-treated children. The incidence of cerebral palsy was 10% in the dexamethasone group and 22% in the placebo group. Minor developmental delay was found in 42% of dexamethasone-treated and in 53% of placebo-treated children. Our follow-up results indicate that the beneficial effect of prenatal glucocorticoid treatment on cerebral complications I intraventricular haemorrhage or periventricular leucomalacia) demonstrated during the neonatal period may be followed by a lower incidence of cerebral palsy in surviving premature children. Z Antenatal corricoid. children, dei~elopment, premature
AU - Salokorpi, T
AU - Sajaniemi, N
AU - Hallback, H
AU - Kari, A
AU - Rita, H
AU - von Wendt, L
AU - Sajaniemi N, Salokorpi T
AU - Rita H, Kari A
AU - Randomized, Wendt L
IS - 86
PY - 1997
SP - 294
EP - 298
TI - Randomized study of the effect of antenatal dexamethasone on growth and development of premature children at the corrected age of 2 years
T2 - Acta Paediatrica
ER -
TY - JOUR
AB - Background Synthetic glucocorticoids, to enhance fetal maturation, are a standard treatment when preterm birth before 34 gestational weeks is imminent. While morbidity- A nd mortality-related benefits may outweigh potential neurodevelopmental harms in children born preterm (<37 gestational weeks), this may not hold true when pregnancy continues to term (≥37 gestational weeks). We studied the association of antenatal betamethasone exposure on child mental health in preterm and term children.Methods We included 4708 women and their children, born 2006-2010, from the Prediction and Prevention of Pre-eclampsia and Intrauterine Growth Restriction Study with information on both antenatal betamethasone treatment and child mental and behavioral disorders from the Finnish Hospital Discharge Register from the child's birth to 31 December 2016. Additional follow-up data on mother-reported psychiatric problems and developmental milestones were available for 2640 children at 3.5 (s.d. = 0.07) years-of-age.Results Of the children, 187 were born preterm (61 betamethasone-exposed) and 4521 at term (56 betamethasone-exposed). The prevalence of any mental and behavioral, psychological development, emotional and behavioral, and comorbid disorders was higher in the betamethasone-exposed, compared to non-exposed children [odds ratio 2.76 (95% confidence interval 1.76-4.32), 3.61 (2.19-5.95), 3.29 (1.86-5.82), and 6.04 (3.25-11.27), respectively]. Levels of psychiatric problems and prevalence of

failure to meet the age-appropriate development in personal-social skills were also higher in mother-reports of betamethasone-exposed children. These associations did not vary significantly between preterm and term children.Conclusions Antenatal betamethasone exposure may be associated with mental health problems in children born preterm and in those who end up being born at term.
AU - Wolford, Elina
AU - Lahti-Pulkkinen, Marius
AU - Girchenko, Polina
AU - Lipsanen, Jari
AU - Tuovinen, Soile
AU - Lahti, Jari
AU - Heinonen, Kati
AU - Hämälaïnen, Esa
AU - Kajantie, Eero
AU - Pesonen, Anu Katriina
AU - Villa, Pia M.
AU - Laivuori, Hannele
AU - Reynolds, Rebecca M.
AU - Raïkkönen, Katri
DO - 10.1017/S0033291718004129
IS - 2
KW - Betamethasone
KW - developmental milestones
KW - glucocorticoids
KW - mental health
KW - psychiatric problems
PB - Cambridge University Press
PY - 2019
SP - 247
EP - 257
TI - Associations of antenatal glucocorticoid exposure with mental health in children
T2 - Psychological Medicine
VL - 50
ER -
TY - JOUR
AB - Objectives Antenatal corticosteroids (ACS) decrease neonatal mortality and morbidity among preterm neonates, yet there has been concern regarding their long-term safety. We hypothesised that potential long-term adverse effects of ACS may be observed among infants born during the late preterm period (LPT, 340/7–366/7 weeks of gestation), when the benefits of ACS are subtle. Design Population-based, retrospective cohort. Setting Ontario, Canada, between 2006 and 2011. Patients All live singleton infants born during the LPT period with a minimum 5-year follow-up. Interventions Exposure to ACS prior to 340/7 weeks of gestation. Main outcome measures Suspected neurocognitive disorder, audiometry testing or visual testing. Results Overall, 25 668 infants were eligible for analysis, of whom 2689 (10.5%) received ACS. Infants in the ACS group had lower mean birth weight and higher rates of birth weight <10th percentile, neonatal resuscitation and neonatal intensive care unit admission. At 5 years of age, ACS exposure was associated with an increased risk of suspected neurocognitive disorder (adjusted HR (aHR) 1.12, 95% CI

1.05 to 1.20), audiometry testing (aHR 1.20, 95% CI 1.10 to 1.31) and visual testing (aHR 1.06, 95% CI 1.01 to 1.11). Conclusion In children born during the LPT period, exposure to ACS prior to 340/7 weeks of gestation is associated with an increased utilisation of the healthcare system related to audiometry and visual testing and suspected neurocognitive disorders by 5 years of age.
AU - Aviram, Amir
AU - Murphy, Kellie
AU - McDonald, Sarah
AU - Asztalos, Elizabeth
AU - Zaltz, Arthur
AU - Redelmeier, Donald
AU - Shah, Baiju
AU - Barrett, Jon
AU - Melamed, Nir
DA - 2022/5//
DO - 10.1136/archdischild-2021-322152
IS - 3
PB - BMJ Publishing Group
PY - 2022
SP - F250
EP - F255
TI - Antenatal corticosteroids and neurodevelopmental outcomes in late preterm births
T2 - Archives of Disease in Childhood: Fetal and Neonatal Edition
VL - 107
ER -