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**Date:** 13 December 2017

**Sources Searched:** Embase, Medline

## Coronary Artery Dissection (SCAD) in Pregnancy and the Puerperium

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### **Evidence Summary:**

- Spontaneous coronary artery dissection (SCAD) is the spontaneous separation of the coronary artery wall not iatrogenic or related to trauma. Although rare, it is the most common cause of myocardial infarction in pregnancy or the postpartum period ([Elkayam U et al, 2014](#))
- Spontaneous coronary artery dissection typically affects young females without conventional predisposing factors for atherosclerosis. Pregnancy or the recent postpartum interval is recognized as an associated factor in 12–30% of cases. Risk factors include fibromuscular dysplasia, connective tissue disorders, extreme emotional distress or physical exertion, family history of SCAD. Less frequent risk factors are hypertensive crisis, coronary vasospasm and cocaine abuse. ([Codsí, E et al, 2016](#))
- The aetiology of SCAD is uncertain. Hormonal changes during pregnancy, hemodynamic stress and changes in the autoimmune status have been considered as possible etiological factors ([Sheik, A.S. 2012](#)).
- The estimated 10-year recurrence rate of spontaneous coronary artery dissection is 29% ([Tweet, M.S. 2012](#))

## **1. Repeat Coronary Artery Dissection in Pregnancy: A Case Report and Review of the Literature.**

**Author(s):** Bitting, Casey P; Zumwalt, Ross E

**Source:** Journal of forensic sciences; Sep 2017; vol. 62 (no. 5); p. 1389-1394

**Publication Date:** Sep 2017

**Publication Type(s):** Case Reports

**PubMedID:** 28168688

Available at [Journal of forensic sciences](#) - from Wiley Online Library Science , Technology and Medicine Collection 2017

**Abstract:**Non-atherosclerotic spontaneous coronary artery dissection (NA-SCAD) is a rare cause of morbidity and mortality with a propensity for young, healthy, and often peripartum women. NA-SCAD etiology is poorly understood, with possible hormonal and hereditary mechanisms. Current treatment strategies range from conservative management (often showing resolution on angiographic follow-up) to invasive angiographic procedures. Rarely, NA-SCAD has recurred in another coronary artery, ranging hours to years later. We report NA-SCAD of the right coronary artery (RCA) in a 30-year old, 3-month postpartum female with an additional autopsy finding of remote myocardial infarction (MI) in the left anterior descending (LAD) coronary artery territory. The remote MI is consistent with prior NA-SCAD of the LAD and, given the medical history, may have occurred in the peripartum period of the decedent first pregnancy 3 years earlier. As such, to the best of our knowledge, this may represent the first reported case of NA-SCAD recurrence in a subsequent pregnancy.

**Database:** Medline

## **2. Spontaneous Coronary Artery Dissection and Pregnancy.**

**Author(s):** Naderi, Sahar

**Source:** Current treatment options in cardiovascular medicine; Sep 2017; vol. 19 (no. 9); p. 69

**Publication Date:** Sep 2017

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

**PubMedID:** 28780663

Available at [Current Treatment Options in Cardiovascular Medicine](#) - from SpringerLink

**Abstract:**OPINION STATEMENTSpontaneous coronary artery dissection (SCAD) is a non-atherosclerotic, non-traumatic cause of coronary artery dissection. SCAD is the most common cause of myocardial infarction in pregnancy or the postpartum period and results in significant cardiovascular morbidity and mortality in the pregnant population. It is important to consider pregnancy-associated spontaneous coronary artery dissection (PASCAD) high on the differential for a pregnant woman who presents with symptoms consistent with acute coronary syndrome. Management of these patients requires a thoughtful, multidisciplinary approach, with consideration of conservative management if possible. Counseling regarding future pregnancies is also critical and requires compassionate care. Given our limited understanding of SCAD, including PASCAD, more data and research are needed to help guide diagnosis, management, and determination of prognosis.

**Database:** Medline

### 3. Spontaneous Coronary Artery Dissection Associated With Pregnancy.

**Author(s):** Tweet, Marysia S; Hayes, Sharonne N; Codsi, Elisabeth; Gulati, Rajiv; Rose, Carl H; Best, Patricia J M

**Source:** Journal of the American College of Cardiology; Jul 2017; vol. 70 (no. 4); p. 426-435

**Publication Date:** Jul 2017

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

**PubMedID:** 28728686

Available at [Journal of the American College of Cardiology](#) - from ProQuest (Hospital Premium Collection) - NHS Version

**Abstract:**BACKGROUND Spontaneous coronary artery dissection (SCAD) is the most common cause of pregnancy-associated myocardial infarction and remains poorly characterized. OBJECTIVE This study sought to assess presentation, clinical factors, and outcomes of pregnancy-associated spontaneous coronary artery dissection (P-SCAD) compared with spontaneous coronary artery dissection not associated with pregnancy (NP-SCAD). METHOD SA Mayo Clinic registry was established in 2010 to include comprehensive retrospective and prospective SCAD data. Records were reviewed to identify women who were pregnant or  $\leq 12$  weeks postpartum at time of SCAD. Complete records were available for 323 women; 54 women met criteria for P-SCAD (4 during pregnancy) and they were compared with 269 women with NP-SCAD. RESULTS Most events occurred within the first month postpartum (35 of 50). Compared with NP-SCAD, P-SCAD patients more frequently presented with ST-segment elevation myocardial infarction (57% vs. 36%;  $p = 0.009$ ), left main or multivessel SCAD (24% vs. 5%;  $p < 0.0001$ ; and 33% vs. 14%;  $p = 0.0027$ , respectively), and left ventricular function  $\leq 35\%$  (26% vs. 10%;  $p = 0.0071$ ). Among women with imaging of other vascular territories, P-SCAD was less likely with a diagnosis of fibromuscular dysplasia and extracoronary vascular abnormalities (42% vs. 64%;  $p = 0.047$ ; and 46% vs. 77%;  $p = 0.0032$ , respectively). Compared with U.S. birth data, women with P-SCAD were more often multiparous ( $p = 0.0167$ ), had a history of infertility therapies ( $p = 0.0004$ ), and had pre-eclampsia ( $p = 0.001$ ). On long-term follow-up (median 2.3 years) recurrent SCAD occurred in 51 patients, with no difference in the Kaplan Meier 5-year recurrence rates (10% vs. 23%;  $p = 0.18$ ). CONCLUSION SP-SCAD patients had more acute presentations and high-risk features than women with NP-SCAD did. The highest frequency of P-SCAD occurred during the first postpartum month and P-SCAD patients less often had extracoronary vascular abnormalities. Hormonal, hemodynamic variations, and yet-undefined mechanisms might be significant contributors to P-SCAD. (The "Virtual" Multicenter Spontaneous Coronary Artery Dissection [SCAD] Registry [SCAD]; NCT01429727; Genetic Investigations in Spontaneous Coronary Artery Dissection [SCAD]; NCT01427179).

**Database:** Medline

#### **4. Pregnancy-Related Spontaneous Coronary Artery Dissection: A Case Series and Literature Review.**

**Author(s):** Rose, Emily; Gedela, Maheedhar; Miller, Nathan; Carpenter, Paul L

**Source:** The Journal of emergency medicine; Jun 2017; vol. 52 (no. 6); p. 867-874

**Publication Date:** Jun 2017

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

**PubMedID:** 28396082

**Abstract:**BACKGROUND Cardiac emergencies during pregnancy are rare but have significant associated morbidity and mortality when they do occur. The emergency physician must not only be aware of potentially life-threatening conditions in the pregnant woman, but also know the emergent management and treatment of these conditions to avoid worsening of the underlying condition. Pregnancy-related spontaneous coronary artery dissection has been described in the cardiology literature, but is not well-known in emergency medicine literature.CASE SERIESWe present a case series of six previously healthy women ages 27 to 39 years who presented 1 to 75 days after delivery with spontaneous coronary artery dissection. The left main coronary was involved in 5 of 6 cases. One patient died, 5 survived. Two survivors maintained significant long-term disability. The patient that died had the diagnosis made on autopsy, the others were diagnosed with coronary angiography. Two patients were treated with stents, 2 with coronary artery bypass surgery, and 2 with medical management. WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?: Emergent coronary catheterization is indicated if this diagnosis is suspected. However, emergency care teams must also understand how and why management including coronary artery catheterization can exacerbate the underlying condition. The role of coronary artery computed tomography remains unknown, although it exposes the fetus to significant radiation if the woman is still pregnant at presentation. Medical management is indicated with diffuse or distal disease as pregnancy-related coronary artery dissections often resolve with time. Localized discrete lesions may be stented. Coronary artery bypass graft surgery may be considered if the left main artery is involved or there are multiple proximal lesions. Cardiac transplantation is indicated rarely.

**Database:** Medline

## **5. Pregnancy and the Risk of Spontaneous Coronary Artery Dissection: An Analysis of 120 Contemporary Cases.**

**Author(s):** Havakuk, Ofer; Golan, Sorel; Mehra, Anil; Elkayam, Uri

**Source:** Circulation. Cardiovascular interventions; Mar 2017; vol. 10 (no. 3)

**Publication Date:** Mar 2017

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

**PubMedID:** 28302642

Available at [Circulation. Cardiovascular interventions](#) - from Ovid (LWW Total Access Collection 2015 - Q1 with Neurology)

**Abstract:**BACKGROUND Because of the rarity of this condition, information on pregnancy-associated spontaneous coronary artery dissection is limited. We reviewed a large number of contemporary pregnancy-associated spontaneous coronary artery dissection cases in an attempt to define the clinical characteristics and provide management recommendations. METHODS AND RESULTS A literature search for cases of pregnancy-associated spontaneous coronary artery dissection reported between 2000 and 2015 included 120 cases; 75% presented with ST-segment-elevation myocardial infarction, and 80% had anterior myocardial infarction. Left anterior descending coronary artery was involved in 72% of cases, left main segment in 36%, and 40% had multivessel spontaneous coronary artery dissection. Ejection fraction was reduced to <40% in 44% of cases. Percutaneous coronary intervention was successful in only 50% of cases. Coronary artery bypass surgery was performed in 44 cases because of complex anatomy, hemodynamic instability, or failed percutaneous coronary intervention. Maternal complications included cardiogenic shock (24%), mechanical support (28%), urgent percutaneous coronary intervention (28%), urgent coronary artery bypass surgery (27.5%), maternal mortality (4%), and fetal mortality (2.5%). During follow-up for 305±111 days, there was a high incidence of symptoms because of persistent or new spontaneous coronary artery dissections, and 5 women needed heart transplantation or ventricular assist device implantation. CONCLUSIONS Pregnancy-associated spontaneous coronary artery dissection is commonly associated with left anterior descending, left main, and multivessel involvement, which leads to a high incidence of reduced ejection fraction, and life-threatening maternal and fetal complications. Percutaneous coronary intervention is associated with low success rate and high likelihood of complications, and coronary artery bypass surgery is often required. Recurrent ischemic events because of persistent or new spontaneous coronary artery dissection are common during long-term follow-up.

**Database:** Medline

## 6. Coronary artery dissection in the puerperium: Case report and literature review

**Author(s):** Tahmasebi F.; Hurrell A.; Gupta M.

**Source:** BJOG: An International Journal of Obstetrics and Gynaecology; Mar 2017; vol. 124 ; p. 87-88

**Publication Date:** Mar 2017

**Publication Type(s):** Conference Abstract

**Abstract:**Background Spontaneous coronary artery dissection (SCAD) is a rare but vitally important cause of acute coronary syndrome. Its preponderance for women and particularly women during the peripartum period signifies that all healthcare professionals caring for this cohort of the population should have a sound understanding of the condition. Aetiology remains poorly understood, but may represent eosinophilic inflammatory infiltration of vessel walls or defects in collagen. The exceedingly high mortality rate necessitates prompt diagnosis, usually by angiography - diagnosis has been made all too often at autopsy in the past. There is no one-size-fits-all treatment; management must be individualised according to haemodynamic status and affected vessel(s) and may include conservative management, percutaneous coronary intervention or bypass grafting. Recovery may be complicated by extension of the haematoma / false lumen, valvular pathology secondary to ischaemia and sudden cardiac death, and close postoperative surveillance is mandatory. Here, we present a case report of a 41-year-old lady who had SCAD two weeks postpartum, complicated by ischaemic papillary rupture and mitral regurgitation requiring mechanical valve replacement. Additionally, we present a review of the current literature on SCAD, including management and critical analysis potential complications.

**Database:** EMBASE

## 7. Pregnancy-associated spontaneous coronary artery dissection: insights from a case series of 13 patients.

**Author(s):** Cade, Jamil R; Szarf, Gilberto; de Siqueira, Maria Eduarda M; Chaves, Áurea; Andréa, Júlio C M; Figueira, Hélio R; Gomes, Manuel M; Freitas, Bárbara P; Filgueiras Medeiros, Juliana; Dos Santos, Márcio Ricardo; Fiorotto, Walter B; Daige, Augusto; Gonçalves, Rosaly; Cantarelli, Marcelo; Alves, Cláudia Maria Rodrigues; Echenique, Leandro; de Brito, Fábio S; Perin, Marco A; Born, Daniel; Hecht, Harvey; Caixeta, Adriano

**Source:** European heart journal cardiovascular Imaging; Jan 2017; vol. 18 (no. 1); p. 54-61

**Publication Date:** Jan 2017

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

**PubMedID:** 26928981

Available at [European Heart Journal Cardiovascular Imaging](#) - from Oxford Journals - Medicine

**Abstract:**AIMS We sought to present a series of 13 pregnancy-associated spontaneous coronary artery dissection (P-SCAD), their angiographic and multimodal imaging findings, acute phase treatment, and outcomes. METHODS AND RESULTS Between 2005 and 2015, 13 cases of P-SCAD were collected from a database of 11 tertiary hospitals. The mean age was  $33.8 \pm 3.7$  years; most patients had no risk factors for coronary artery disease, and the majority were multiparous. P-SCAD occurred during the puerperium in 12 patients with a median time of 10 days. Only one patient presented with P-SCAD in the 37th week of pregnancy, and she was the only patient who died in this series. Six patients (46%) presented with ST-segment elevation acute myocardial infarction (STEMI), six (46%) presented with non-STEMI, and one presented with unstable angina; one-third of women had cardiogenic shock. In 12 patients, the dissection involved the left anterior descending or circumflex artery, and it extended to the left main coronary artery in 6 patients. Intravascular ultrasound or

optical coherence tomography helped to confirm diagnosis and guide treatment in 46% of cases. Seven women were managed clinically; percutaneous coronary intervention was performed in five cases, and coronary artery bypass grafting was performed in one patient. **CONCLUSION** In these 13 cases of P-SCAD, clinical presentation commonly included acute myocardial infarction and cardiogenic shock. Multivessel dissections and involvement of the left coronary artery and left main coronary artery were highly prevalent. Clinicians must be aware of angiographic appearances of P-SCAD for prompt diagnosis and management in these high-risk patients.

**Database:** Medline

## **8. A nationwide evaluation of spontaneous coronary artery dissection in pregnancy and the puerperium.**

**Author(s):** Faden, Majed S; Bottega, Natalie; Benjamin, Alice; Brown, Richard N

**Source:** Heart (British Cardiac Society); Dec 2016; vol. 102 (no. 24); p. 1974-1979

**Publication Date:** Dec 2016

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

**PubMedID:** 27411842

Available at [Heart](#) - from BMJ Journals - NHS

**Abstract:** **OBJECTIVE** Spontaneous coronary artery dissection (SCAD) is a rare and potentially lethal cause of myocardial infarction (MI). The purpose of our study was to estimate the prevalence and maternal outcomes of pregnancies complicated by SCAD. **MATERIALS AND METHODS** A population-based cohort study on all births identified in the Healthcare Cost and Utilization Project from 2008 to 2012. Disease prevalence was calculated and logistic regression was used to estimate the adjusted odds ratio (aOR) for risk factors and different maternal complications. **RESULTS** A total of 4 363 343 pregnancy-related discharges were evaluated. 79 cases of SCAD were identified resulting in a prevalence of 1.81 per 100 000 pregnancies. The mean maternal age at the time of diagnosis was 33.4 years ( $\pm 5.2$ ). Chronic hypertension (aOR, 2.67; 95% CI 1.18 to 6.03), lipid profile abnormalities (aOR, 48.22; 95% CI 24.25 to 95.90), chronic depression (aOR, 3.56; 95% CI 1.43 to 8.83) and history of migraine (aOR, 3.93; 95% CI 1.52 to 10.17) were associated with an elevated risk for SCAD. MI was diagnosed in 66 (85.5%) cases of SCAD with anterior and subendocardial territories being the most common locations. Thirty one patients (40%) with SCAD underwent angioplasty with the majority receiving stents, which was associated with a longer hospital stay than those treated conservatively or with bypass. **CONCLUSION** SCAD is a rare aetiology of MI; risk factors and outcomes are illustrated in the current study. The puerperium is an important period for the development of pregnancy-related SCAD. Careful evaluation of pregnant and postpartum women with chest pain is warranted, especially if these risk factors are identified.

**Database:** Medline

### **9. Spontaneous Coronary Artery Dissection in Pregnancy: What Every Obstetrician Should Know.**

**Author(s):** Codsì, Elisabeth; Tweet, Marysia S; Rose, Carl Hans; Arendt, Katherine W; Best, Patricia J M; Hayes, Sharonne N

**Source:** Obstetrics and gynecology; Oct 2016; vol. 128 (no. 4); p. 731-738

**Publication Date:** Oct 2016

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

**PubMedID:** 27607875

Available at [Obstetrics and Gynecology](#) - from Ovid (LWW Total Access Collection 2015 - Q1 with Neurology)

**Abstract:**Spontaneous coronary artery dissection is a major cause of myocardial infarction in pregnancy and the postpartum period. It occurs predominantly in young women with few or no conventional risk factors for atherosclerosis and has been clinically underrecognized. Treatment differs from that of myocardial infarction as a result of atherosclerosis and the diagnosis should be considered in all parturient and postpartum patients with acute coronary syndrome. Complications of spontaneous coronary artery dissection include recurrence, congestive heart failure, and death. Thus, specialist obstetrician-gynecologists and maternal-fetal medicine specialists need to gain knowledge of spontaneous coronary artery dissection to improve outcomes.

**Database:** Medline

### **10. Pregnancy-related spontaneous coronary artery dissection.**

**Author(s):** Regitz-Zagrosek, Vera; Jaguszewska, Kinga; Preis, Krzysztof

**Source:** European heart journal; Sep 2015; vol. 36 (no. 34); p. 2273-2274

**Publication Date:** Sep 2015

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

**PubMedID:** 26594680

Available at [European Heart Journal](#) - from Oxford Journals - Medicine

**Database:** Medline



### **11. Postpartum Spontaneous Coronary Artery Dissection An Uncommon Cause of Acute Coronary Syndrome.**

**Author(s):** Raizada, Amol; Petrasko, Marian

**Source:** South Dakota medicine : the journal of the South Dakota State Medical Association; Jul 2015; vol. 68 (no. 7); p. 300-302

**Publication Date:** Jul 2015

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

**PubMedID:** 26267930

**Abstract:**Spontaneous coronary artery dissection (SCAD) is an uncommon cause of acute coronary syndrome (ACS) that tends to affect young females. Diagnosis is confirmed by a dissection flap that is seen on coronary angiogram in the absence of underlying coronary atherosclerosis. New techniques in intra-coronary imaging such as intravascular ultrasound (IVUS) and optical coherence tomography (OCT) are useful in diagnosing SCAD. These techniques are helpful because SCAD is often associated with intra-mural hematoma within the vessel wall that would not be visualized on coronary angiography. Given the lack of randomized trials, most data on treatment of this relatively uncommon condition is controversial and based on expert opinion. Postpartum SCAD comprises a small subgroup of all patients presenting with SCAD.

**Database:** Medline

### **12. Emergent cesarean section in the catheterization laboratory for spontaneous coronary artery dissection.**

**Author(s):** Sundaram, Varun; Chaudhry, Sunit-Preet; Reddy, Yogesh N V; Longenecker, Chris T; Fang, James C

**Source:** The American journal of cardiology; Jun 2015; vol. 115 (no. 12); p. 1777-1778

**Publication Date:** Jun 2015

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

**PubMedID:** 25888300

Available at [American journal of cardiology](#) - from ProQuest (Hospital Premium Collection) - NHS Version

**Abstract:**Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome in pregnant women. Delay in the diagnosis might lead to substantial maternal and fetal morbidity and mortality. Although there have been reports of SCAD in pregnancy, to our knowledge, there have been no reports of maternal and fetal hemodynamic compromise related to SCAD leading to emergent delivery of fetus in the cardiac catheterization laboratory.

**Database:** Medline

**13. Pregnancy after spontaneous coronary artery dissection: a case series.**

**Author(s):** Tweet, Marysia S; Hayes, Sharonne N; Gulati, Rajiv; Rose, Carl H; Best, Patricia J M

**Source:** Annals of internal medicine; Apr 2015; vol. 162 (no. 8); p. 598-600

**Publication Date:** Apr 2015

**Publication Type(s):** Research Support, Non-u.s. Gov't Letter

**PubMedID:** 25894037

Available at [Annals of internal medicine](#) - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location] : Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.

**Database:** Medline

**14. Multivessel spontaneous dissection of the left coronary tree in the postpartum period: case report and review of the literature.**

**Author(s):** Petrou, E; Bousoula, E; Boutsikou, M; Iakovou, I; Kolovou, G; Pavlides, G

**Source:** European review for medical and pharmacological sciences; 2014; vol. 18 (no. 24); p. 3743-3746

**Publication Date:** 2014

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

**PubMedID:** 25555861

**Abstract:**Spontaneous coronary artery dissection is a rare cause of myocardial infarction predominantly associated with young women during the third trimester of pregnancy or during the postpartum period. Multivessel spontaneous coronary artery dissection is an even less frequent condition with limited reports in medical literature. Hormonal changes as well as hemodynamic stress are some of the factors that have been implicated in the etiology of this condition. However, the exact pathophysiological process leading to spontaneous coronary artery dissection has not yet been elucidated. The spectrum of clinical presentation ranges from mild symptoms to cardiac arrest. Herein, we report the case of a 39-year-old woman with spontaneous two coronary vessel dissection during her postpartum period presented with ST elevation myocardial infarction on electrocardiogram complicated with pulmonary edema and cardiorespiratory arrest.

**Database:** Medline

**15. Pregnancy-related spontaneous coronary artery dissection**

**Author(s):** Vijayaraghavan R.; Verma S.; Gupta N.; Saw J.

**Source:** Circulation; 2014; vol. 130 (no. 21); p. 1915-1920

**Publication Date:** 2014

**Publication Type(s):** Article

**PubMedID:** 25403597

Available at [Circulation](#) - from HighWire - Free Full Text

Available at [Circulation](#) - from Ovid (LWW Total Access Collection 2015 - Q1 with Neurology)

**Database:** EMBASE

#### **16. Editorial: Spontaneous coronary artery dissection in pregnancy**

**Author(s):** Kawagoe T.

**Source:** Journal of Cardiology Cases; Apr 2014; vol. 9 (no. 4); p. 168-169

**Publication Date:** Apr 2014

**Publication Type(s):** Editorial

**Database:** EMBASE

#### **17. The risk of pregnancy after spontaneous coronary artery dissection**

**Author(s):** Tweet M.S.; Hayes S.; Gulati R.; Best P.

**Source:** Journal of the American College of Cardiology; Apr 2014; vol. 63 (no. 12)

**Publication Date:** Apr 2014

**Publication Type(s):** Conference Abstract

Available at [Journal of the American College of Cardiology](#) - from ProQuest (Hospital Premium Collection) - NHS Version

Available at [Journal of the American College of Cardiology](#) - from Free Medical Journals . com

**Abstract:**Background: Spontaneous coronary artery dissection (SCAD) is an important cause of myocardial infarction (MI) in young patients. In women, approximately 20% occur in the peripartum period. This and the 20% recurrence rate in long-term follow-up evoke concern for pregnancy after SCAD. Thus, the usual recommendation is to advise against it even though data assessing this risk are lacking. Methods: We evaluated all women enrolled in a SCAD registry at the Mayo Clinic. The diagnosis of SCAD was confirmed by coronary angiography. Women who had pregnancies after the index SCAD were identified from questionnaires and medical records. Clinical data, outcomes of previous and subsequent pregnancies, knowledge of SCAD diagnosis prior to the pregnancy, and extracoronary vascular conditions, including fibromuscular dysplasia, were evaluated. Subsequent events, pregnancy outcome, and recurrent SCAD were assessed. Results: A total of 7 of the 266 women in the registry had a pregnancy after an initial SCAD (2.6%). Mean age at the index SCAD was 35.5 years, with 43% occurring in the postpartum period. Mean age at the subsequent pregnancy was 37 years. Only 4 women knew that the initial event was SCAD at the time of pregnancy. The other 3 had been given an initial diagnosis of coronary vasospasm. Six pregnancies resulted in live births, with 1 miscarriage at 15 weeks. In follow-up, 6/7 did not have SCAD-related complications, while 1 patient had recurrent SCAD at 9 weeks postpartum resulting in an ST-elevation MI involving the left main coronary artery, treated with emergent coronary artery bypass surgery. This patient's index SCAD was not related to pregnancy. Conclusion: The risk of recurrent SCAD in women who become pregnant after an initial SCAD is notable and can be devastating. Importantly, just under half of the women had received an incorrect diagnosis of the cause of her MI rather than SCAD, which may have altered decision-making regarding further pregnancies. Thus, reproductive age women with a history of MI should have careful re-evaluation of etiology with an emphasis on accurately identifying SCAD in order for these women to make an informed decision before subsequent pregnancies.

**Database:** EMBASE

### **18. Spontaneous peripartum coronary artery dissection presentation and outcome.**

**Author(s):** Higgins, George L; Borofsky, Jennifer S; Irish, Christine B; Cochran, Thomas S; Strout, Tania D

**Source:** Journal of the American Board of Family Medicine : JABFM; 2013; vol. 26 (no. 1); p. 82-89

**Publication Date:** 2013

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

**PubMedID:** 23288285

Available at [Journal of the American Board of Family Medicine](#) - from HighWire - Free Full Text

Available at [Journal of the American Board of Family Medicine](#) - from Free Medical Journals . com

**Abstract:**OBJECTIVEThe objective of this study was to determine whether spontaneous peripartum coronary artery dissection (SPCAD) is a cause of acute myocardial infarction in women.METHODSPatients with SPCAD reported in the recent literature were analyzed to elucidate the clinically relevant characteristics of this condition.RESULTSForty-seven cases of SPCAD are described. Patient characteristics include the following: mean age,  $33.5 \pm 5.2$  years; gravity, 2.7 (95% confidence interval, 1.8-3.5); mean gestational age if prepartum,  $32.5 \pm 4.2$  weeks (range, 23-36 weeks); and mean onset if postpartum,  $22.9 \pm 26.1$  days (range, 3-90 days). Only 17 patients (36%) reported a cardiac risk factor, with the most frequent being smoking. All presented with characteristic ischemic pain; 25% of patients were hemodynamically unstable; and 81% of initial electrocardiograms demonstrated ST-elevation myocardial infarctions. The left coronary artery system was involved 81% of the time. Thirty percent of patients were managed conservatively or with thrombolytic therapy, whereas 34% received emergent percutaneous cardiac intervention and 36% required bypass surgery. There were no maternal deaths. Long-term follow-up revealed good cardiac function in the majority of patients, although 3 women required heart transplantation.CONCLUSIONSSPCAD can occur weeks before or after delivery and should be considered in women presenting during the peripartum period with acute chest pain.

**Database:** Medline

### **19. Cocaine-induced postpartum coronary artery dissection: a case report and 80-year review of literature.**

**Author(s):** Katikaneni, Pavan K; Akkus, Nuri I; Tandon, Neeraj; Modi, Kalgi

**Source:** The Journal of invasive cardiology; Aug 2013; vol. 25 (no. 8); p. E163

**Publication Date:** Aug 2013

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

**PubMedID:** 23913612

**Abstract:**The incidence of cocaine-induced myocardial infarction (MI) in pregnancy is unknown. During the peripartum period, cocaine-abusing women are highly susceptible to MI caused by the effect of cocaine on a heart that is already stressed by hemodynamic changes of pregnancy. MI is an infrequent event during pregnancy and the peripartum period, with an estimated rate of 1 in 16,000 patients. Spontaneous coronary artery dissection (SCAD) can account for up to 27% of pregnancy-related MIs. We describe a case of MI diagnosed by increased troponin I levels in a postpartum patient with recent crack cocaine use in the setting of SCAD that required percutaneous coronary intervention of the left anterior descending and diagonal arteries. We also provide a comprehensive review of published literature related to this clinical entity.

**Database:** Medline

## **20. Postpartum spontaneous dissection of the first obtuse marginal branch of the left circumflex coronary artery causing acute coronary syndrome: a case report and literature review.**

**Author(s):** Shahzad, Khurram; Cao, Long; Ain, Quara Tul; Waddy, Jennifer; Khan, Nawazish; Nekkanti, Rajasekhar

**Source:** Journal of medical case reports; Mar 2013; vol. 7 ; p. 82

**Publication Date:** Mar 2013

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

**PubMedID:** 23510019

Available at [Journal of Medical Case Reports](#) - from BioMed Central

Available at [Journal of Medical Case Reports](#) - from Europe PubMed Central - Open Access

**Abstract:**INTRODUCTIONSpontaneous coronary artery dissection is a rare but important cause of acute coronary syndrome. It can cause unstable angina, acute myocardial infarction, and sudden death. The condition commonly affects young females with about one-third of the cases occurring during pregnancy and the peripartum period. The diagnosis may occasionally be overlooked as the patients are often young and have no risk factors for coronary artery disease.CASE PRESENTATIONHere we report the case of a 29-year-old African American woman who presented with acute coronary syndrome due to spontaneous dissection of the first obtuse marginal branch of the left circumflex coronary artery at three weeks post-partum and recovered requiring only medical management, possibly by longitudinal distribution of the intramural hematoma leading to good distal flow.CONCLUSIONSSpontaneous coronary artery dissection should be suspected in all young multiparous females presenting with chest pain in the peripartum period even in the absence of risk factors. Urgent diagnosis by angiography is required. It is recommended that treatment should be tailored to meet individual circumstances. Patients who present with single-vessel disease and hemodynamic stability, and who receive medical treatment with anticoagulation, nitrates and a beta-blocker, should experience good results.

**Database:** Medline

## **21. Myocardial infarction in pregnancy and postpartum in the UK.**

**Author(s):** Bush, N; Nelson-Piercy, C; Spark, P; Kurinczuk, J J; Brocklehurst, P; Knight, M; UKOSS

**Source:** European journal of preventive cardiology; Feb 2013; vol. 20 (no. 1); p. 12-20

**Publication Date:** Feb 2013

**Publication Type(s):** Research Support, Non-u.s. Gov't Journal Article

**PubMedID:** 22127355

**Abstract:**AIMCardiac disease is a leading cause of maternal death in the developed world, responsible for one-fifth of all maternal deaths in the UK. The aim of this study was to estimate the incidence of myocardial infarction (MI) in pregnancy and up to one week postpartum in the UK and describe risk factors, management and outcomes.METHODSA prospective population-based study with nested case control analysis used the UK Obstetric Surveillance System to identify all women in the UK with MI in pregnancy (in the years 2005-2010). A control group of 1360 women was used for comparison. Multivariable unconditional logistic regression was conducted to identify potential risk factors for MI in pregnancy and calculate adjusted odds ratios with 95% confidence intervals.RESULTSTwenty-five cases of MI in pregnancy were reported, giving an estimated incidence of 0.7 per 100,000 maternities (95%CI 0.5-1.1). Maternal age, smoking, hypertension, twin pregnancy and pre-eclampsia were independently associated with MI in pregnancy. Fifteen (60%) women underwent coronary angiography; nine (60%) had coronary atherosclerosis, three (21%) had coronary artery dissection, one (7%) had a coronary thrombus and two (13%) had normal coronary

arteries. Nine women had angioplasty +/- stenting and two were thrombolysed. No women died. **CONCLUSIONS** Many risk factors are both recognisable and modifiable. Management of MI in pregnancy was highly variable indicating a clear need for further information regarding the safety and outcomes of different interventions. The addition of pregnancy status as a compulsory field in cardiac audit databases would enable routine collection of this information.

**Database:** Medline

## **22. Challenges in the management of postpartum spontaneous coronary artery dissection**

**Author(s):** Truesdell A.G.; Delgado G.A.; Li J.; Abbott J.D.; Atalay M.K.; Singh A.K.

**Source:** Interventional Cardiology (London); Jun 2012; vol. 4 (no. 3); p. 371-386

**Publication Date:** Jun 2012

**Publication Type(s):** Review

Available at [Interventional Cardiology](#) - from ProQuest (Hospital Premium Collection) - NHS Version

**Abstract:** Spontaneous coronary artery dissection (SCAD) is a rare event, disproportionately affecting young women free of atherosclerotic risk factors in the peripartum period. The pathophysiology of peripartum SCAD and how it differs from other forms is not well understood. Fewer than 500 cases of SCAD have been reported in the literature worldwide, only a fraction of which have occurred in peripartum patients. This single-center case series of five postpartum SCAD patients with longitudinal follow-up, along with a review of the literature, presents a diverse set of complications and management strategies and highlights the challenges in caring for these patients in the absence of robust clinical data or consensus guidelines. © 2012 Future Medicine Ltd.

**Database:** EMBASE

### **23. Pregnancy-related Spontaneous Coronary Artery Dissection: Two Case Reports and a Comprehensive Review of Literature.**

**Author(s):** Sheikh, Azeem S; O'Sullivan, Michael

**Source:** Heart views : the official journal of the Gulf Heart Association; Apr 2012; vol. 13 (no. 2); p. 53-65

**Publication Date:** Apr 2012

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

**PubMedID:** 22919449

Available at [Heart views : the official journal of the Gulf Heart Association](#) - from Europe PubMed Central - Open Access

Available at [Heart views : the official journal of the Gulf Heart Association](#) - from ProQuest (Hospital Premium Collection) - NHS Version

**Abstract:**Spontaneous coronary artery dissection is a rare cause of acute coronary syndrome, particularly seen in women during pregnancy or in the puerperium. It has a high acute phase mortality. The etiology is uncertain. Hormonal changes during pregnancy, hemodynamic stress and changes in the autoimmune status have been considered as possible etiological factors. A timely diagnosis and institution of appropriate treatment is important for a successful outcome. There is no consensus of opinion for optimal treatment. Conservative management, coronary artery bypass graft surgery, and percutaneous coronary intervention, all have been described in the literature as possible therapeutic options. Spontaneous coronary artery dissection should be considered as a differential in any young woman presenting with chest pain associated with pregnancy. We report two cases of pregnancy-associated spontaneous coronary artery dissection, both successfully managed, along with a comprehensive review of the previously published literature.

**Database:** Medline

### **24. Presentation and therapy of spontaneous coronary artery dissection and comparisons of postpartum versus nonpostpartum cases.**

**Author(s):** Ito, Hiroki; Taylor, Lee; Bowman, Martha; Fry, Edward T A; Hermiller, James B; Van Tassel, James W

**Source:** The American journal of cardiology; Jun 2011; vol. 107 (no. 11); p. 1590-1596

**Publication Date:** Jun 2011

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

**PubMedID:** 21439531

**Abstract:**Predisposing risk factors, clinical course, and prognosis of spontaneous coronary artery dissection (SCAD) remain poorly understood. We reviewed medical records and coronary angiograms of patients admitted to our institution with the diagnosis of SCAD from 1999 through 2010. A definite diagnosis of SCAD required the agreement of 2 blinded board-certified interventional cardiologists who reviewed all images separately. Baseline characteristics of patients (n = 23) included mean age  $45 \pm 11$  years, female gender in all (100%), history of hypertension in 13 (57%), and postpartum in 7 (30%). Eleven (48%) had ST-segment elevation on initial electrocardiogram. SCAD involved the left main in 5 patients (21.7%), left anterior descending coronary artery in 16 (70%), left circumflex coronary artery in 8 (35%), and right coronary artery in 6 (26%). Four patients (17%) underwent coronary stenting and 6 (26%) required urgent bypass surgery. Comparison between postpartum and nonpostpartum patients revealed significant differences in mean peak troponin levels:  $50 \pm 34$  ng/ml vs  $21 \pm 23$ ,  $p = 0.04$ , mean left ventricular ejection fraction:  $34 \pm 6\%$  vs  $49 \pm 9\%$ ,  $p < 0.01$ , proximal coronary segment distribution: 6 (86%) vs 3



(19%),  $p = 0.004$ , and left anterior descending coronary artery distribution: 7 (100%) vs 9 (56%),  $p = 0.04$ , respectively. Repeat coronary angiographies were performed in 11 patients (46%) during a mean follow-up of  $39 \pm 38$  months and 10 (91%) were found to have healed SCAD, including those who had undergone bypass surgery. In conclusion, our patients with SCAD were characterized by female gender, absence of coronary risk factors, and a high rate of vascular healing without residual stenosis. Larger infarct was found in postpartum patients.

**Database:** Medline

## **25. Recurrent post-partum coronary artery dissection.**

**Author(s):** Rajab, Taufiek K; Khalpey, Zain; Kraemer, Bernhard; Resnic, Frederic S; Gallegos, Robert P

**Source:** Journal of cardiothoracic surgery; Oct 2010; vol. 5 ; p. 78

**Publication Date:** Oct 2010

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

**PubMedID:** 20932332

Available at [Journal of Cardiothoracic Surgery](#) - from BioMed Central

Available at [Journal of Cardiothoracic Surgery](#) - from ProQuest (Hospital Premium Collection) - NHS Version

**Abstract:**Coronary artery dissection is a rare but well-described cause for myocardial infarction during the post-partum period. Dissection of multiple coronary arteries is even less frequent. Here we present a case of recurrent post-partum coronary artery dissections. This unusual presentation poses unique problems for management. A 35 year-old female, gravida 3 para 2, presented with myocardial infarction 9 weeks and 3 days post-partum. Cardiac catheterization demonstrated left anterior descending (LAD) dissection but an otherwise normal coronary anatomy. The lesion was treated with four everolimus eluting stents. Initially the patient made an unremarkable recovery until ventricular fibrillation arrest occurred on the following day. Unsynchronized cardioversion restored a normal sinus rhythm and repeat catheterization revealed new right coronary artery (RCA) dissection. A wire was passed distally, but it was unclear whether this was through the true or false lumen and no stents could be placed. However, improvement of distal RCA perfusion was noted on angiogram. Despite failure of interventional therapy the patient was therefore treated conservatively. Early operation after myocardial infarction has a significantly elevated risk of mortality and the initial dissection had occurred within 24 hours. This strategy proved successful as follow-up transthoracic echocardiography after four months demonstrated a preserved left ventricular ejection fraction of 55-60% without regional wall motion abnormalities. The patient remained asymptomatic from a cardiac point of view.

**Database:** Medline



## **26. Contemporary management of pregnancy-related coronary artery dissection: A single-centre experience and literature review**

**Author(s):** Appleby C.E.; Barolet A.; Ing D.; Ross J.; Schwartz L.; Seidelin P.; Silversides C.; Horlick E.

**Source:** Experimental and Clinical Cardiology; 2009; vol. 14 (no. 1)

**Publication Date:** 2009

**Publication Type(s):** Review

**Abstract:** Spontaneous coronary artery dissection (SCAD) is an infrequent event that is most commonly associated with pregnant women or those in the postpartum period. Because of its rarity, the literature describing this condition is confined to sporadic case reports, with few reporting long-term follow-up, and no clear consensus exists on the optimal treatment strategy for these patients. The present article reports a single-centre experience with SCAD, highlighting the issues surrounding its management with a brief description of five cases of pregnancy-associated coronary dissection. The treatment used in these cases ranged from a conservative medical approach to surgical and percutaneous intervention, with one patient proceeding to transplantation. Four of the cases have long-term angiographic follow-up. In addition, a comprehensive review of all previously published cases is presented, and temporal trends in the management strategy are highlighted. Possible pathophysiological mechanisms pertaining to this condition, and the complex diagnostic and therapeutic issues involved, which may affect both patient and fetus, are discussed. Finally, an optimal approach to patients with SCAD, informed by our experience and literature review, is described. © 2009 Pulsus Group Inc. All rights reserved.

**Database:** EMBASE

## **27. Postpartum coronary artery dissection**

**Author(s):** Collyer M.; Bellenger N.; Nachimuthu P.; Parasuraman R.; Taylor M.J.O.

**Source:** Journal of Obstetrics and Gynaecology; May 2008; vol. 28 (no. 4); p. 451-453

**Publication Date:** May 2008

**Publication Type(s):** Article

**PubMedID:** 18604695

**Database:** EMBASE

## **28. Pregnancy-associated spontaneous coronary artery dissection.**

**Author(s):** Goland, Sorel; Schwarz, Ernst R; Siegel, Robert J; Czer, Lawrence S C

**Source:** American journal of obstetrics and gynecology; Dec 2007; vol. 197 (no. 6); p. e11

**Publication Date:** Dec 2007

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

**PubMedID:** 18060935

**Abstract:** Spontaneous coronary artery dissection is a rare cause of acute myocardial infarction that occurs particularly in women during the pregnancy and in the postpartum period. We describe a dramatic case of pregnancy-related spontaneous left main coronary artery dissection that resulted in acute myocardial infarction with severe left ventricular dysfunction and was complicated by acute heart failure and cardiogenic shock. Urgent revascularization and restoration of myocardial perfusion that were performed in this case resulted in marked left ventricular function recovery and clinical improvement.

**Database:** Medline

## **29. Postpartum dissection of the left main coronary artery.**

**Author(s):** Rogers, Ian S; Rinaldi, Michael J; Humphrey, Chester B; Boden, William E; Dougherty, James E

**Source:** Clinical cardiology; Apr 2006; vol. 29 (no. 4); p. 175-178

**Publication Date:** Apr 2006

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

**PubMedID:** 16649728

Available at [Clinical cardiology](#) - from IngentaConnect - Open Access

**Abstract:** Peripartum coronary artery dissection is rare, but it is an increasingly recognized risk to women of childbearing age. Literature reviews reveal that about 80% of the population with spontaneous coronary artery dissections (SCAD) are female, and approximately 25-33% of cases occurred while the woman was pregnant or in the peripartum phase. Most cases have presented within 2 weeks of delivery. The left anterior descending is the most commonly affected vessel. The etiology is poorly understood, but many reports suggest that SCAD occurs as a result of protease release secondary to an eosinophilic vasculitis resulting in vessel lysis. Many investigators have examined the correlation between peripartum SCAD and estrogen levels; however, case studies have shown conflicting results regarding estrogen levels as the putative causative factor. Optimal treatment remains controversial. Presently, stenting appears to be best employed in the patients who have single-vessel dissection not involving the left main coronary artery (LMCA). Surgical revascularization via coronary artery bypass graft remains the optimal therapy in patients whose dissection involves the LMCA, in patients with concurrent multivessel dissection, and in patients with disease refractory to medical management. It is important to consider coronary artery dissection in the differential of any young woman who presents with signs or symptoms consistent with acute coronary syndrome, particularly if she is peripartum. Furthermore, once suspected, it is imperative that a definitive diagnostic study, that is, coronary angiography, be completed prior to the initiation of treatment whenever possible.

**Database:** Medline

### **30. Spontaneous coronary artery dissection postpartum**

**Author(s):** Juszczuk M.; Marnejon T.; Hoffman D.A.

**Source:** Journal of Invasive Cardiology; Sep 2004; vol. 16 (no. 9); p. 524-526

**Publication Date:** Sep 2004

**Publication Type(s):** Article

**PubMedID:** 15353812

**Database:** EMBASE

### **31. Coronary artery dissection during pregnancy.**

**Author(s):** Esinler, Ibrahim; Yigit, Nuray; Ayhan, Ali; Kes, Sirri; Aytemir, Kudret; Acil, Tayfun

**Source:** Acta obstetricia et gynecologica Scandinavica; Feb 2003; vol. 82 (no. 2); p. 194-196

**Publication Date:** Feb 2003

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

**PubMedID:** 12648186

Available at [Acta obstetricia et gynecologica Scandinavica](#) - from Wiley Online Library Science , Technology and Medicine Collection 2017

**Database:** Medline

### **32. Coronary artery dissection during pregnancy and the postpartum period: two case reports and review of literature.**

**Author(s):** Koul, A K; Hollander, G; Moskovits, N; Frankel, R; Herrera, L; Shani, J

**Source:** Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions; Jan 2001; vol. 52 (no. 1); p. 88-94

**Publication Date:** Jan 2001

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

**PubMedID:** 11146532

Available at [Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions](#) - from Wiley Online Library Science , Technology and Medicine Collection 2017

**Abstract:**Spontaneous coronary dissection is a rare event occurring particularly in women during the peripartum and postpartum period. Two cases related to the early postpartum period with a successful outcome are described, together with a comprehensive review of all the previously published cases. Diagnostic and therapeutic considerations of this unique clinical entity are discussed and reviewed.

**Database:** Medline

### **33. Review and hypothesis: the eosinophil and peripartum heart disease (myocarditis and coronary artery dissection)--coincidence or pathogenetic significance?**

**Author(s):** Borczuk, A C; van Hoeven, K H; Factor, S M

**Source:** Cardiovascular research; Mar 1997; vol. 33 (no. 3); p. 527-532

**Publication Date:** Mar 1997

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

**PubMedID:** 9093522

Available at [Cardiovascular research](#) - from Oxford Journals - Medicine

**Abstract:**OBJECTIVETo examine a possible relationship between peripartum heart disease (myocarditis and spontaneous coronary dissection) and the presence of eosinophils.BACKGROUNDEosinophils have been shown to have potential collagenolytic and cytotoxic activity. Eosinophils may play a role in postpartum uterine involution. The presence of eosinophils in spontaneous coronary dissection and myocarditis in the postpartum period raises the possibility of a role for eosinophils in these diseases.METHODSWe reviewed the files of one of us (S.M.F.) for cases of peripartum myocarditis and spontaneous coronary dissection and assessed the frequency of eosinophilic inflammation. Seventeen postpartum myocarditis and/or cardiomyopathy cases were found and two spontaneous coronary dissections. Fifteen sex- and age-matched controls on non-postpartum myocarditis and borderline myocarditis were evaluated and eosinophil counts per unit area compared. Also, a Medline search of all previously published cases of spontaneous coronary dissection was performed back to 1966.RESULTSO f the 16 heart biopsies and one autopsy in the peripartum period, 10 were shown to contain easily identified eosinophils (6 myocarditis, 1 borderline, 3 cardiomyopathy). When presence of eosinophils was compared with the control group, a statistically significant difference was obtained ( $P = 0.036$ ). The two new spontaneous coronary dissection cases had eosinophils along the dissection plane; the literature search produced 13 of 24 autopsied peripartum spontaneous coronary dissections with eosinophils for a total of 15 of 26 with our cases.CONCLUSIONSAn association exists between eosinophils and peripartum cardiac disease (myocarditis and spontaneous coronary dissection). The role of eosinophils in labor, uterine involution and collagenolysis and the possible relation to cardiac disease are discussed.

**Database:** Medline

## Strategy 334245

#	Database	Search term	Results
1	Medline	("coronary artery dissection").ti,ab	1226
2	Medline	(pregnan*).ti,ab	433742
3	Medline	exp PREGNANCY/	821223
5	Medline	(Puerperium).ti,ab	5547
6	Medline	("postpartum period").ti,ab,af	26320
7	Medline	(2 OR 3 OR 5 OR 6)	919098
8	Medline	(1 AND 7)	214
9	EMBASE	("coronary artery dissection").ti	1266
10	EMBASE	*"CORONARY ARTERY DISSECTION"/	905
11	EMBASE	(9 OR 10)	1487
12	EMBASE	(pregnan*).ti,ab	569710
13	EMBASE	exp PREGNANCY/	686722
14	EMBASE	(Puerperium).ti,ab	6193
15	EMBASE	exp PUERPERIUM/	55992
16	EMBASE	("post partum" OR postpartum).ti,ab	68343
17	EMBASE	(12 OR 13 OR 14 OR 15 OR 16)	932613
18	EMBASE	(11 AND 17)	306
19	EMBASE	18 [English language]	286