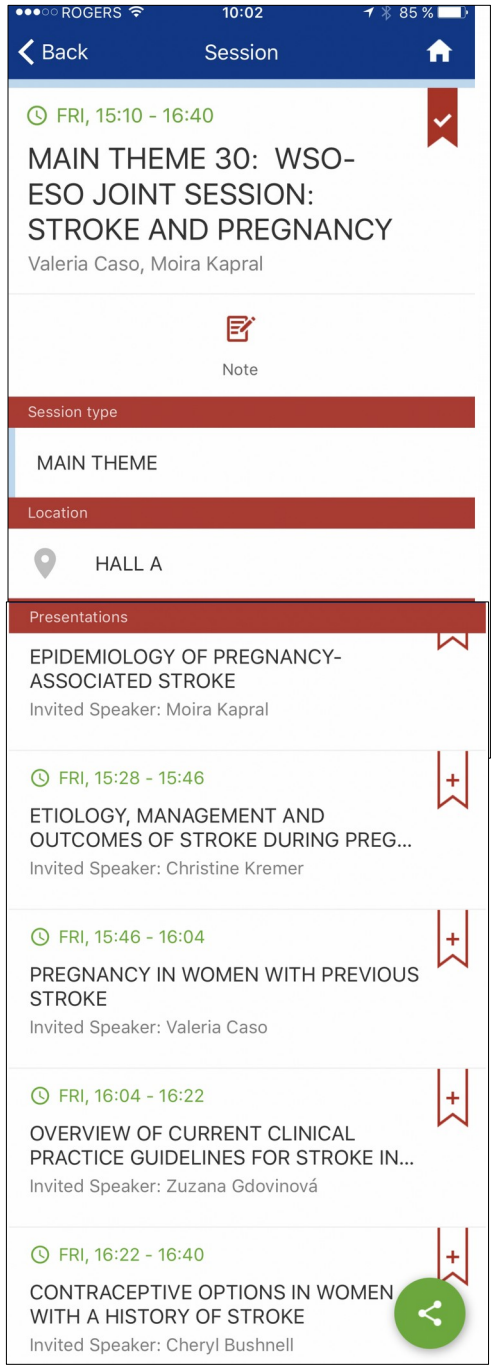

AVC et Grossesse:
Quels sont les enjeux?

Ariane Mackey MD FRCP(C) Neurologue
CHU de Québec / Hôpital de l'Enfant-Jésus
Professeure agrégée de médecine
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15 h 35 **AVC et Grossesse : Quels sont les enjeux?**

Dre Ariane Mackey, neurologue, CHU de Québec – Hôpital de l'Enfant-Jésus

Objectifs :

- Connaître les points saillants du Consensus canadien sur le traitement de l'AVC aigu durant la grossesse.
- Savoir rechercher les causes d'AVC plus spécifiquement reliées à la grossesse.
- Réviser les traitements antithrombotiques indiqués et contre indiqués en prévention d'AVC durant la grossesse.

AVC et Grossesse: A. Mackey

Conflits d'intérêts potentiels

Aucun lié au contenu de cette conférence

AVC reliés à la grossesse: EPIDÉMIO

AVC: 25-34/100,000 vs 11/100,00 pour 15-45 ans non reliés

- Artériels ou Veineux
- Ischémiques ou Hémorrhagiques

- Antepartum: 40-45%
- Péripartum: 2-3%
- Postpartum: ad 6 semaines: 50-55%

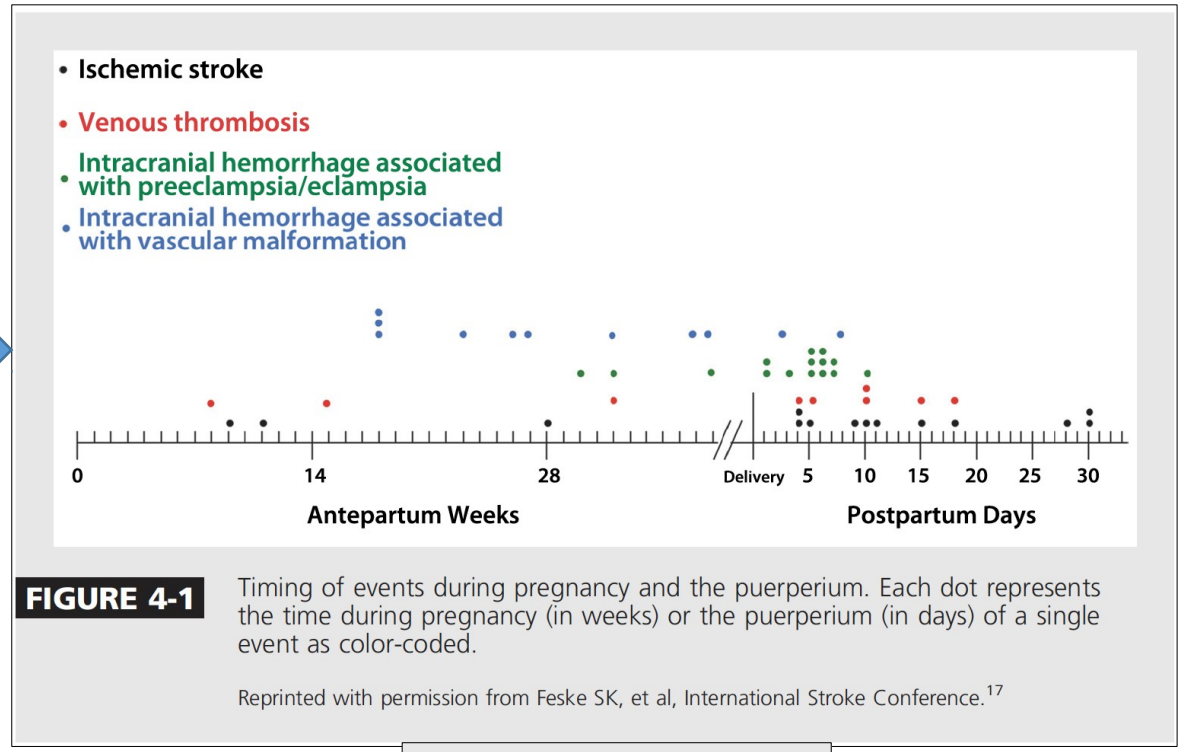


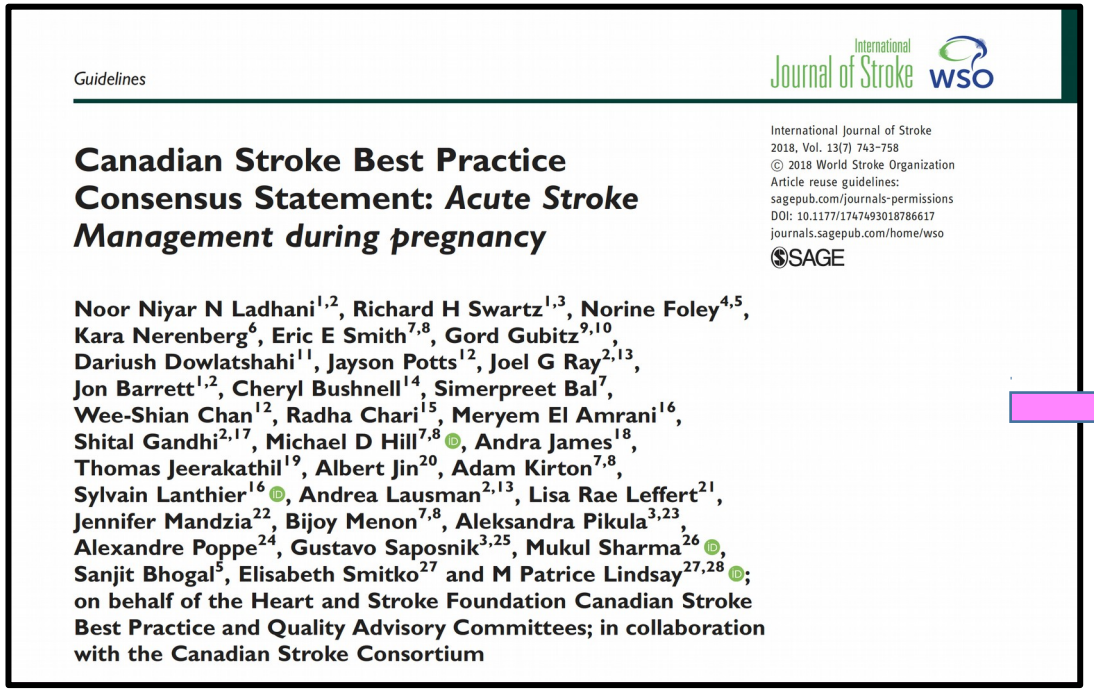
FIGURE 4-1 Timing of events during pregnancy and the puerperium. Each dot represents the time during pregnancy (in weeks) or the puerperium (in days) of a single event as color-coded.

Reprinted with permission from Feske SK, et al, International Stroke Conference.[17]

Continuum (Minneap Minn) 2014;20(1):80–99.

AVC AIGU et Grossesse:

Quels sont les enjeux?



Guidelines

International Journal of Stroke WSO

Canadian Stroke Best Practice Consensus Statement: *Acute Stroke Management during pregnancy*

International Journal of Stroke
2018, Vol. 13(7) 743–758

DOI: 10.1177/1747493018786617
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Noor Niyar N Ladhani[1,2], Richard H Swartz[1,3], Norine Foley[4,5], Kara Nerenberg[6], Eric E Smith[7,8], Gord Gubitz[9,10], Dariush Dowlatshahi[11], Jayson Potts[12], Joel G Ray[2,13], Jon Barrett[1,2], Cheryl Bushnell[14], Simerpreet Bal[7], Wee-Shian Chan[12], Radha Chari[15], Meryem El Amrani[16], Shital Gandhi[2,17], Michael D Hill[7,8], Andra James[18], Thomas Jeerakathil[19], Albert Jin[20], Adam Kirton[7,8], Sylvain Lanthier[16], Andrea Lausman[2,13], Lisa Rae Leffert[21], Jennifer Mandzia[22], Bijoy Menon[7,8], Aleksandra Pikula[3,23], Alexandre Poppe[24], Gustavo Saposnik[3,25], Mukul Sharma[26], Sanjit Bhogal[5], Elisabeth Smitko[27] and M Patrice Lindsay[27,28]; on behalf of the Heart and Stroke Foundation Canadian Stroke Best Practice and Quality Advisory Committees; in collaboration with the Canadian Stroke Consortium

Contrairement au CSBPR (guidelines aigu):

- pas de niveau d'évidence assigné
- la plupart des rec. sont basées sur l'opinion des experts

Contient 9 sections (boites)

Toutes les décisions nécessitent l'évaluation des risques vs bénéfices pour la mère et le fœtus; en général on priorise la mère et on prend des décisions similaires à celles des jeunes femmes non enceintes..
Ref.. au guidelines « standard »

1.0 Initial emergency management

i. Where possible, rapid access to a stroke center should be sought for all pregnant women with suspected acute stroke. Guidelines for acute stroke management outside the context of pregnancy can be found at www.strokebestpractices.ca, and these guidelines should be followed except when necessary to modify and/or individualize for maternal considerations and fetal safety.
   a. Acute stroke management decisions should be based on stroke type, severity of symptoms, medical condition of the patient, and, when available, consideration of the personal values and wishes of the patient and family members or next-of-kin.
   b. Institutions with both obstetrical and stroke specialization should have protocols in place for rapid assessment and access to appropriate pregnancy and stroke-related diagnostic tests and interventions.
   c. Management of acute stroke in pregnant women should reflect collaboration between stroke teams and obstetrics teams. Rapid involvement of both teams is important to ensure the best possible outcomes for the pregnant woman and the fetus.
   d. Institutions that lack either obstetrical care or neurologic specialists should predefine pathways and protocols for emergent collaborative management in person or through telemedicine modalities and consider transfer to a center with appropriate neurological and obstetrical expertise, if needed.
   e. Education and coordination of care between the emergency department, obstetrics, stroke, and radiology services should be in place to ensure a stroke during pregnancy is considered an emergency and to facilitate access to rapid intervention. The risks of delayed stroke care should be understood at all institutions caring for pregnant women. As well arrangements should be in place to ensure an acknowledgment of the urgency in the management of severe preeclampsia with neurologic features.
   f. Protocols and educational efforts should be in place to help practitioners collaborate and manage pregnant or peripartum patients with either neurologic signs and symptoms and/or in the setting of possible severe preeclampsia.

ii. Protocols for rapid brain and vascular imaging will help identify an acute stroke and inform stroke etiology which may guide management (e.g. stroke secondary to preeclampsia vs. due to an arterial occlusion vs. other causes).
   a. Focal neurologic deficits are usually not part of preeclampsia and represent an emergency mandating interdisciplinary care. Since stroke can be secondary to preeclampsia, the presence of focal neurological deficits should alert obstetrical practitioners to the possibility of acute stroke.
   b. Protocols should be in place to acutely manage severe hypertension (i.e. sBP $\geq$ 160 mmHg or dBP $\geq$ 110 mmHg). In the setting of preeclampsia or severe hypertension with neurological symptoms, the goal is to achieve an urgent and sustained reduction of systolic and diastolic blood pressure to less than 160/110 mmHg to reduce the risk of maternal stroke.[10,14,15]
   c. The impact of blood pressure reduction on placental perfusion should be considered. Obstetrics/Maternal Fetal Medicine practitioners should be involved in ongoing assessments of the maternal-placental-fetal unit and decision-making related to blood pressure lowering and the approach to fetal monitoring and surveillance where appropriate. Care must be taken to not cause hypotension or hypoperfusion.[14,16]
   d. Protocols for magnesium sulfate administration in cases of severe preeclampsia, to reduce the risk of eclampsia, should be in place to help standardize and facilitate rapid care in these cases.

Boite no !: Se roder d'avance…

Etablir la collaboration avec équipe d'**obstétrique**, d'urgence, de radiologie
Mettre en place les divers protocoles incluant:
- Imagerie et autres habituels
- Traitement HTA en évitant hypotension..
- Monitoring foetal
- Magnésium en cas de préeclamsie
- Test de grossesse prn
- - reconnaitre les « red flags », ex: céphalée aiguë

De : Ariane Mackey
Envoyé : 5 novembre 2018 13:06

Objet : stroke- grossesse

Bonjour [redacted]

Je présente dur l'AVC vs grosesse à la SSVQ le 16 nov à MTL

Comme vous le savez des guidelines canadiens sont sortis pour cette chose en mai ou juin
Je me demandais advenant un cas d'AVC aigu chez une femme enceinte si on a un "set up" quelqu'onque avec l'obstétrique

Est-ce que un obstétricien du CHU peut venir ici rapidement et monitorer adéquatement le bébé et possiblement faire une césarienne d'urgence ici disons préthombectomie ?

ou gerer une hémorrhagie utérine post thrombolyse et per ou pré thrombectomie ??
merci de m'éclairer la dessus si possible.... et en espérant que ca n'arrivera pas :)

AM
Ariane Mackey, MD FRCP (C) neurologue
Professeur agrégé de médecine,
Directrice du Centre de Recherche en Neurovasculaire
CHU de Québec / Hôpital de l'Enfant-Jésus

Boite no 2: IMAGERIE DIAGNOSTIQUE en AIGU

2.0 Diagnostic imaging

Refer to CSBPR Acute Stroke Management module, section 4 for additional information on initial imaging of a suspected stroke patient (www.strokebestpractices.ca).

i. Counseling of pregnant patients on imaging-associated risk for both mother and fetus may be considered and coordinated between clinical and imaging teams.
Note: Many clinicians remain overly concerned about the fetal risk associated with neuroimaging and ionizing radiation (CT). The fetal dose of radiation, and corresponding risk, associated with neuroimaging is extremely small.[21]

ii. Where an acute stroke is suspected, given the severe maternal risk caused by potential delay in diagnosis when compared to the minimal risk to the fetus with CT imaging, it is acceptable to conduct a CT scan of the head without first establishing pregnancy.

a. For severe disabling stroke, standard of care for the diagnosis of acute stroke includes immediate imaging of both the brain and cerebrovascular system, *within minutes* of hospital arrival.
Note: In patients displaying mild or transient stroke symptoms who are not being considered for emergent stroke intervention, brain imaging and vessel imaging should still be undertaken in accordance with timelines as defined in CSBPR Acute Stroke Management section 2.

b. In most centers, this is achieved with immediate CT with CT angiography (CTA) of the head and neck. In some cases, CT Perfusion (CTP) or MRI may also be used to identify potential candidates for intravenous thrombolysis with alteplase and/or acute endovascular thrombectomy. Both CTA and CTP use intravenous contrast and have higher doses of radiation than a CT head.

c. In the time-sensitive emergency of severe disabling stroke, the health of the mother is paramount and CT with contrast is often the most accessible option to determine if patients are eligible for acute endovascular thrombectomy.
- Where immediately available as part of a local acute stroke protocol, MRI of the brain with time-of-flight (non-contrast) imaging of the blood vessels may be used in place of CT/CTA to visualize the brain and vasculature *(Refer to iii below)*.
- In select cases (e.g. presence of a hyperdense middle cerebral artery on non-contrast CT), CTA may be deferred in a pregnant woman in favor of moving directly to digital subtraction angiography for potential treatment of a proximal occlusion appropriate to explain the symptoms.

d. Based on currently available evidence, the ionizing radiation associated with non-contrast CT head in pregnant patients does not expose the fetus to the high levels of radiation associated with increased risks of abortion, malformation, or other adverse pregnancy outcomes.[19,20]
- A typical CT of the mother's head carries a fetal radiation dose exposure of 0.001 mGy. The typical occupational limit for fetal radiation is 5 mGy. Therefore, the fetal exposure from a maternal CT head is 5000 times less than the allowable occupational exposure and carries negligible risks for fetal malformation, abortion, or other pregnancy complications when compared to the general risks of pregnancy.[22–24]
- A typical CT head exposes the fetus to a negligible amount of radiation. Owing to the distance of the mother's head away from the uterus, there is a low amount of scatter and minimal fetal exposure.
- If CT scanning is used, efforts to minimize radiation exposure such as shielding of the abdomen/pelvis and minimizing extra scans are encouraged.

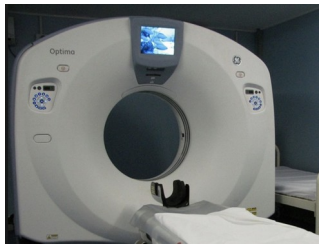
e. There is a lack of available evidence on any known harm identified in human or animal studies of exposure to CT contrast dye.
- For breastfeeding, less than 1% of CT contrast dye is excreted in breast milk; of that, less than 1% is absorbed in infant gastrointestinal tract. Continuation of breastfeeding after exposure to CT contrast dye is reasonable.

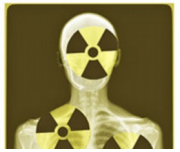
iii. MRI, without gadolinium, does not expose the mother or fetus to ionizing radiation. When appropriate and available, and where the results can assist in clinical decision-making, MRI is therefore a reasonable option in pregnancy. *However, in many centers, MRI is not readily and rapidly available; in the setting of disabling acute stroke, the most available imaging modality should be utilized to avoid delaying treatment.*

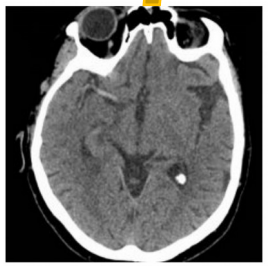
a. Time of flight imaging modalities (non-contrast MR angiography or venography) can often provide sufficient vascular information for emergency stroke decision-making in pregnancy and is preferred over contrast scanning.

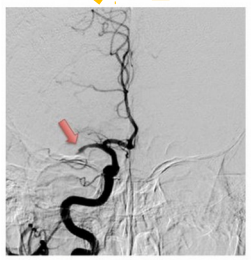
b. MRI at 1.5 or 3.0 tesla (T) without gadolinium does not increase the risk of adverse fetal outcomes, whether exposure occurs in the first trimester[18] or later.[19] MRI of the fetus has been shown to be safe in the second and third trimesters.[25]

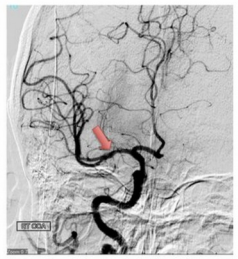
c. Gadolinium exposure in the first trimester may be associated with an increased risk of adverse outcomes.[18] Even outside of pregnancy, gadolinium is rarely needed in the setting of acute stroke diagnosis. Therefore, gadolinium is not recommended for stroke assessment in women with known pregnancy.











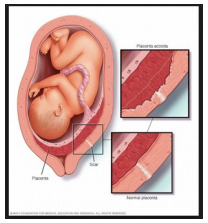
AVC aigu majeur: … "standard of care…" CT et CTA

- Radiations ionisantes d'un CT tête ne seraient pas associées à une augmentation du risque d'avortement ou malformations
  - Exposion foetale serait négligeable 0.001mGy
  - CTA: plus de radiations, mais peu d'info sur risques réels
  - Pour le contraste; moins de 1% est excrété dans lait maternel et de ce montant moins de 1% est absorbé via le tractus GI de l'enfant, donc PAS contre indication

- IRM si rapidement accessible peut être considéré
  - mais **éviter le gadolinium**

- Dans cas sélectionnés ex: MCA hyperdense; **CTA peu être remplacé par angio IA directement pour thrombectomie probable**

THROMBOLYSE durant la grossesse



3.0 Acute ischemic stroke treatment: intravenous thrombolysis and endovascular treatment

Refer to CSBPR 2018 Acute Stroke Management module, section 5 for administration of hyperacute stroke treatments for ischemic stroke. All consensus statements in this section are aligned to these recommendations.

3.1 Intravenous alteplase

i. Acute stroke treatment decisions should be based on severity of symptoms, medical condition of the patient, and, when available, consideration of the personal values and wishes of the patient and her family or next-of-kin.

ii. Treatment options for a pregnant woman with an acute stroke should promptly be considered in consultation with an interdisciplinary team with expertise in neurology, obstetrics and gynecology, maternal-fetal medicine, and interventional radiology, where possible and available.

iii. Acute intravenous thrombolysis with alteplase has been shown to reduce morbidity in the non-pregnant population. There are a limited number of case reports published using alteplase during pregnancy.[36,40]

iv. It is reasonable to consider giving IV alteplase to a pregnant patient with disabling ischemic stroke who meets existing criteria for thrombolysis. The risk–benefit considerations can be complex in the setting of pregnancy; thus, the decision should be undertaken in consultation with a physician with experience in acute stroke treatment either in person or through telestroke modalities.[41,42]
Refer to CSBPR Acute Stroke Management module, section 5 for administration of acute stroke treatments for ischemic stroke.

a. While there are risks of hemorrhage (intracranial and otherwise) from intravenous alteplase, the decision to administer acute thrombolysis should be based on the maternal risks associated with the acute stroke.
b. Placental abruption can occur with or without alteplase, and it is not known whether alteplase increases the risk of abruption. Close monitoring and prompt recognition is important.
c. Alteplase is a large molecule (59,000 daltons) and does not cross the placenta.[43] Therefore, alteplase is not expected or known to pose direct intracranial or systemic bleeding risks to the fetus.
d. The safety and efficacy of intravenous alteplase in the early postpartum period (<14 days after delivery), especially related to risk of maternal postpartum hemorrhage, have not been well established.
   - Case reports suggest that bleeding risk may be increased after alteplase administration and may be further increased if given following Cesarean delivery. Maternal risk of postpartum hemorrhage should be balanced with the risk of a thromboembolic event.[37]
   - The literature to guide assessment of risks from epidural or spinal anesthesia after alteplase administration is limited, but risks of bleeding complications may be increased.

Note: Intravenous alteplase is listed with the Food and Drug Administration (FDA) *as pregnancy category "C" according to the package label, indicating "possible risk" only. There are limited case reports (approximately 30 at time of publication) of IV alteplase in pregnancy for stroke and other conditions, but only one case of fetal demise due to abruption. Other, more common causes of fetal demise in these case reports are related to spontaneous or planned abortion which may also be related to the underlying illness.*

- … consulter équipe inter disciplinaire "back up" obstétrical
- Nombre limités de cas publiés (approx 30) mais outcomes de ceux ci favorables

- ***Il est <u>raisonnable de considérer</u> donner TPA IV a une femme enceinte qui rencontre les critères existants de thrombolyse***

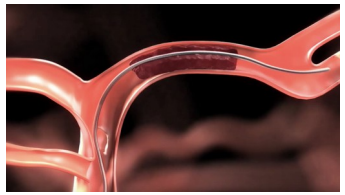
  - Alteplase ne traverve pas barrière placentaire donc <u>pas de risque de saignement chez le foetus</u>

  - On ne sait pas si le TPA entraine un risque accru de <u>décollement placentaire</u>, car ce dernier peut survenir sans thrombolyse

  - La sécurité de la thrombolyse IV en <u>post partum précoce</u>: (moins de 14 jours) n'est pas établie
    - risque de saignement peut être augmenté post césarienne

*Alteplase : Pas tératogène ni toxique selon études animales

THROMBECTOMIE Mécanique durant la grossesse



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3.2 Endovascular thrombectomy

. Pregnancy should not be considered a contraindication to angiography and endovascular thrombectomy (EVT) for proximal large vessel occlusions causing acute disabling stroke. These cases should be treated according to existing guidelines *(refer to 2018 CSBPR Acute Stroke Management module, section 5 on endovascular thrombectomy)*.

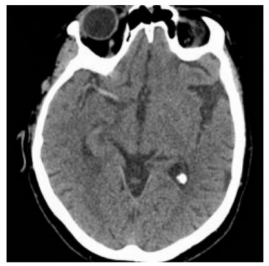
a. Efforts to avoid or reduce the risk of fetal injury such as abdominal shielding and judicious use of x-ray exposures are reasonable.
b. It is not reasonable to delay or defer necessary maternal care for severe disabling stroke secondary to the pregnancy. The acknowledgment of possible fetal risks is appropriate: risks may include radiation and contrast exposure, infections, and arterial puncture complications that could result in both maternal and fetal compromise. However, given the very high morbidity and mortality associated with acute ischemic stroke due to large vessel occlusions, these risks are generally outweighed by the benefits of treatment.

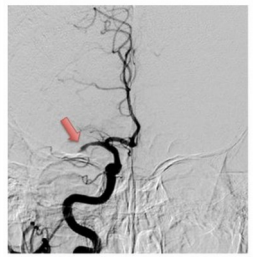
ii. For patients with large vessel occlusions eligible for and with rapid access to endovascular thrombectomy, proceeding directly to endovascular thrombectomy without administering intravenous alteplase could be considered.

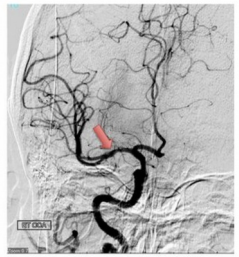
Grossesse

- ***ne devrait pas être considérée une contre-indication*** à l'angiographie et thrombectomie endovasculaire:
- Pour occlusion ***proximale d'un gros*** vaisseau (proximal large vessel occlusion)
- Causant un AVC ***majeur*** (disabling stroke)

Frontière ? Vs petit NIH, M2…







Pour les patientes éligibles:
considérer procéder directement à la thrombectomie ***sans administrer TPA***

Canadian Stroke Best Practice Consensus Statement: *Acute Stroke Management during pregnancy*

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4.0 Management of acute hemorrhagic stroke during pregnancy (SAH, ICH)

5.0 Anesthetic management in the setting of acute stroke during pregnancy

6.0 Early poststroke management in a pregnant woman

7.0 Poststroke antenatal obstetric considerations for women with a stroke in pregnancy

8.0 Intrapartum considerations

9.0 Postpartum management

CAUSES d'AVC durant la grossesse

- <u>Ischémique</u>
- Hémorragique
- Thrombose veineuse

<u>Causes d'AVC chez la jeune adulte non reliées</u>

ASO
Cardioembolic
Lacunaire
Dissection… travail prolongé ?
Autres Vasculopathies; DFM, artérites
Drogues
Migraine
Cryptogénique (ESUS)

*MAV
*Rupture d'anévrysme

*En raison de TA qui augmente après 32 sem et autres changements hémodynamiques

<u>AVC: causes reliées à la grossesse</u>

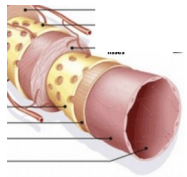
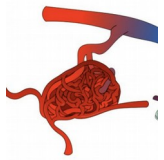
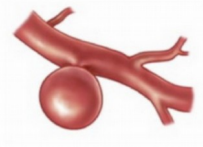
Pré eclampsie:

- **Présente chez 24 - 47% des AVC ischémiques et 14-44% des HIC**
- **Conditions partageant une physiopathologie similaire, avec HTA et dysfonction endothéliale**
  - **Encéphalopathie hypertensive**
  - **PRES**
  - **RCVS**
- **Cardiomyopathie péripartum**
- **Choriocarcinome**
- **Embolie de liquide amniotique**

Changements physiologiques de la grossesse qui augmentent le risque d'AVC

- La grossesse est un état **hypercoagulable** via aug des facteurs procoagulants II, VII, VIII, IX, X, XII, XIII qui résulte en une augmentation de la fibrine
- Ces changements débutents au début de la grossesse et deviennent plus prononcés au **troisième trimestre** ad postpartum afin de limiter les risques de saignement à l'accouchement
- Le trauma de l'accouchement, infections, déshydratation et déficience en fer en PP contribue à **l'état prothrombotique et se poursuit ad 12 sem Post Partum**

- **Volume intravasculaire et « output cardiac »** augmentent vers 25 - 30 semaines et augmente encore durant le travail et l'accouchement et en PP immédiat
- Ces changements hémodynamiques et aussi l'adaptation des changement du tissus conjonctif pourraient rendre les **vaisseaux plus vulnérables** au trauma et à la rupture

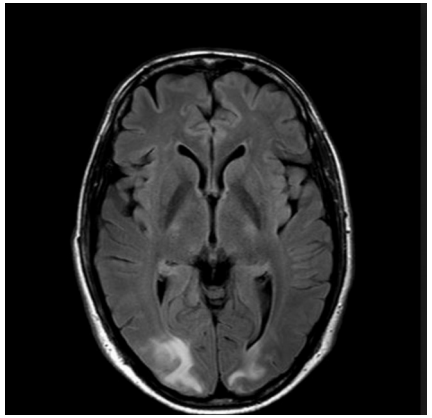




Conditions associées à la **pré-éclampsie** (HTA + protéinurie)

PRES

O'Neal MA, Feske SK. Stroke in pregnancy: a case-oriented review. *Practical Neurology* 2016;**16:**23-34.

- 35 ans G1P0, 32 sem , céphalée sévère ,voit des spots visuels puis perd la vision … aug TA puis Perte de Conscience transitoire
- TA 170/120 , Tx hydralazine et labetalol
- Récupération graduelle de la vision
- Protéinurie 4+
- Bethamathasone et MG IV
- Césarienne
- Jour 2: S/S visuels persistent, CV:N, TA 160/96
- IRM: flair hyperintensités en postérieur (oedeme vasogénique)
- Magnésium IV et nicardipine



- PRES associé à pré-éclampsie serait une manisfestation de pré-éclampsie
- Il n'est pas rare de voir PRES chez patientes en PP qui n'ont jamais eu de pré-éclampsie
- TX; Anti-HTA ; svt labetalol et Mg IV pour la prévention des convulsions

Conditions associées à la **pré-éclampsie** (HTA + protéinurie)

RCVS

O'Neal MA, Feske SK. Stroke in pregnancy: a case-oriented review. *Practical Neurology* 2016;**16**:23-34.

- Deux tiers des RCVS associés à grossesse surviennent dans la première semaine post partum
- Peuvent être déclenché pas Rx vasoactifs; bromocriptine, ergo
- Céphalée thunderclap et démonstration de zones de vasoconstriction / vasodilatation à l'imagerie vasculaire

- Complications
  - **HSA haute convexité : 20-25%**
  - **AVC ischémiques ou hémorrhagiques 5-10%**

- Forte association entre pré-éclampsie et RCVS

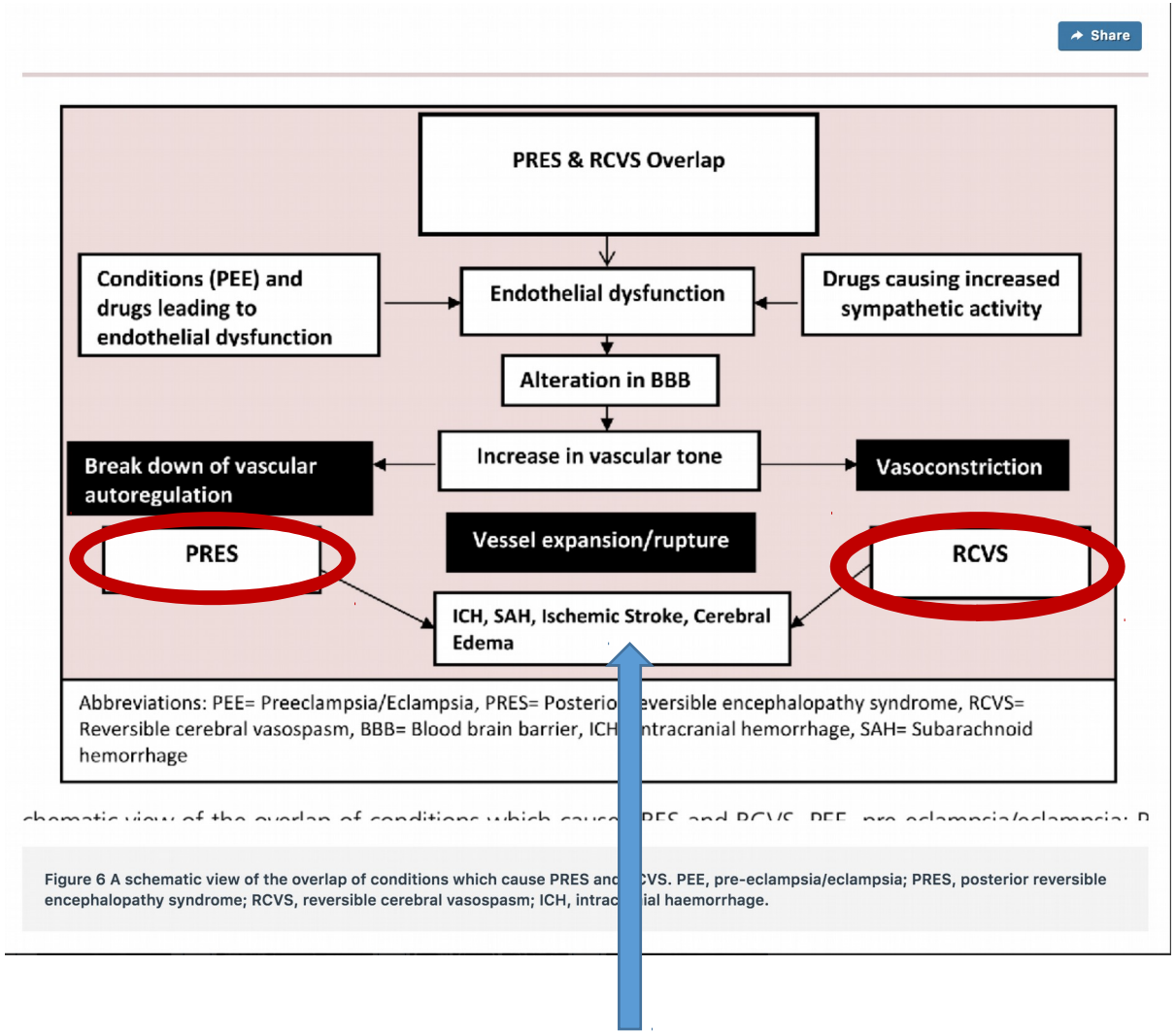


Figure 6 A schematic view of the overlap of conditions which cause PRES and CVS. PEE, pre-eclampsia/eclampsia; PRES, posterior reversible encephalopathy syndrome; RCVS, reversible cerebral vasospasm; ICH, intrac ial haemorrhage.

Conditions associées à la **pré-éclampsie** (HTA + protéinurie)

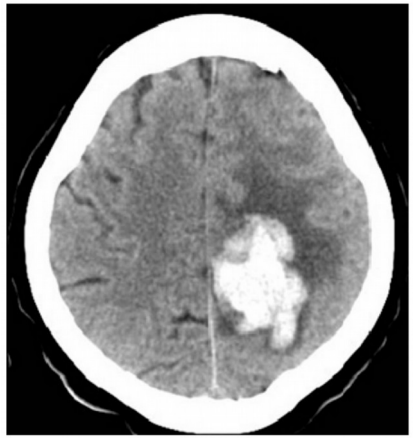
O'Neal MA, Feske SK. Stroke in pregnancy: a case-oriented review. *Practical Neurology* 2016;**16:**23-34.

- 39 ans G6.P1.A4, 33 sem : céphalée sévère N\ V, faiblesse côté droit
- TA 180\100, temp 37.8 , somnolente mais éveillable avec langage normal;
- Agnosie droite-gauche, quadranopsie inf. droite
- Faiblesse droite et néglect, CP ext. à droite

- GB: 15,000, HT 29 (36-46),

- plaquettes dim .: 105
- ALT 125 U/L (5-35), AST 138U/L (15-41)

- Présences de shizocytes, protéinure: 4+



- Pré-éclampsie avec anémie hémolytique, enzymes hépatiques élevés et hypoplaquettose (HELLP) compliqué d'HIP

- HIP peu survenir plus fréquemment ds contexte pré-éclampsie avec ou sans HELLP
- TX: de l'HTA , Mg IV, césarienne urgente

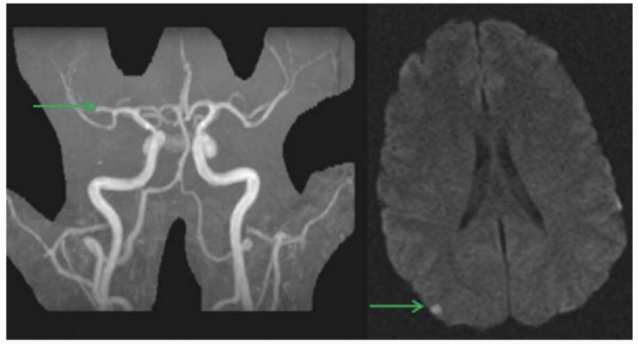
Conditions associées à la **pré-éclampsie**

O'Neal MA, Feske SK. Stroke in pregnancy: a case-oriented review. *Practical Neurology* 2016;**16:**23-34.

- 37 ans, G1P1, une semaine PP, OMI, dyspnée
- Trouble visuel soudain champ inférieur gauche
- IRM petit AVC pariétal droit
- ETT/ETO: dilatation du ventricule gauche avec hypokinésie globale sans thrombus FE: 35%

- Pte anticoagulée au coumadin

- ETO contrôle dans 6 mois: FE: 60-65%



Cardiomyopathie du péripartum (CMP-PP)

Projet de recherhe ICM

- Cardiomyopathie du péripartum
- Peut survenir dans le dernier mois de grossesse jusqu'à 6 mois PP chez femme sans facteurs de risques cardio-vasculaires
- FR:
  - Age maternel plus élevé
  - Grossesses multiples
  - Pré-éclampsie-éclampsie (prévalence quatre fois plus élevé)

- Rôle présumé de la prolactine
- Effet préventif de la bromocriptine postulé et encore étudié

Traitements Antithrombotiques durant la grossesse

Comments and Opinions

Pregnancy, Hormonal Treatments for Infertility, Contraception, and Menopause in Women After Ischemic Stroke

A Consensus Document

Valeria Caso, MD, PhD; Alberto Falorni, MD, PhD; Cheryl D. Bushnell, MD, MHS; Monica Acciarresi, MD; José Remohí, MD; Nikola Sprigg, MbCHB, DM; Sandro Gerli, MD

(*Stroke*. 2017;48:501-506. DOI: 10.1161/STROKEAHA.116.013964.)

Risques de tératogénicité des antithrombotiques

Stroke **February 2017**

Table 2. Associated Teratogenic Risks From Antithrombotic Therapies

Antithrombotic Drugs	Placental Transfer	First Trimester	Second and Third Trimester
Low-dose aspirin (60–150 mg/d)	Yes	Contraindicated (risk of gastroschisis)	Not contraindicated
Other antiplatelets	No data	No data	No data
Warfarin	Yes	Contraindicated (teratogenic)	Not contraindicated
			Regular check of INR
UFH	No	Not contraindicated	Not contraindicated
		Risk of HIT	Risk of HIT
			Regular check of APTT
LMWH	No	Not contraindicated	Not contraindicated
NOAC	Dabigatran: yes	No data	No data
	Rivaroxaban: yes		
	Apixaban: no data		
	Edoxaban: no data		

APTT indicates activated partial thromboplastin time; HIT, heparin-induced thrombocytopenia; INR, international normalized ratio; LMWH, low molecular weight heparin; NOAC, new anticoagulants; and UFH, unfractionated heparin.

(*Stroke*. 2017;48:501-506. DOI: 10.1161/STROKEAHA.116.013964.)

Table 1. Recommendations

Questions	Recommendations	Grade	Level
Point 1: (a) Future pregnancies (b) Secondary prevention	For women with a history of stroke, future pregnancies are not contraindicated based on available data.	2	B
	Pregnant women with defined low-risk condition may be considered for treatment with UFH or LMWH throughout the first trimester, followed by low-dose aspirin for the remainder of the pregnancy	2	B
	In pregnant women with defined low-risk conditions, no recommendations on other types of antiplatelets other than aspirin can be given	2	C
	In pregnant women with defined high-risk conditions, vitamin K antagonists should be avoided between the 6th and 12th weeks of gestation and close to term to avoid the delivery of an anticoagulated fetus. LMWH or UFH should be used either during these above periods alone and alternated with vitamin K antagonists that have the same target INR based on previous prescription or during the entire pregnancy.	2	B
	High-risk condition women on NOAC treatment should be prescribed LMWH or UFH between the 6th and 12th week of gestation, while warfarin can be administered in the other periods. The vitamin K antagonist target INR needs to be based on the underlying pathology. Alternatively, UFH or LMWH may be prescribed throughout pregnancy	2	C
Point 2: Methods of delivery	Natural birth may be preferred to caesarean section. Caesarean section should be performed based on obstetric indications and not on previous history of stroke	2	C
Point 3: Labor induction	When labor is pharmacologically induced, aspirin therapy may be continued	2	C
	Therapeutic doses of UFH/LMWH should be discontinued 24 h prior to inducing labor and restarted within 24 h if no contraindications exist	2	C
	Vitamin K antagonists may be restarted after 24 h after delivery without a loading dose	2	C
Point 4: (a) Breast-feeding during antiplatelet treatment (b) Breast-feeding during anticoagulant treatment	Low-dose aspirin use during breast-feeding may be recommended	2	C
	No recommendations on antiplatelets besides aspirin during breast-feeding can be given	2	C
	Vitamin K antagonist use during breast-feeding may be recommended.	2	C
	UFH/LMH during breast-feeding during breast-feeding may be recommended.	2	C
	NOACs should be avoided during breast-feeding and when necessary substituted with LMWH/ UFH or vitamin K antagonists	2	C
Point 5: Ovarian stimulation	In women with previous stroke, no recommendation on ovarian stimulation could be given	2	C
Point 6: Hormonal contraceptive therapy	OC should not be recommended to women with previous stroke	1	B
Point 7: (a) Hormone replacement therapy and alternative strategies	HRT should not be recommended to women with previous stroke	1	A
	In women with previous stroke Gabapentin may be recommended for hot flashes.	2	C
	In women with previous stroke, no recommendation on the use of SSRI for hot flashes could be given	2	C
	Smoking habit, physical inactivity, and a BMI above normal should be discouraged in menopausal women with previous stroke	2	B

BMI indicates body mass index; HRT, hormone replacement therapy; INR, international normalized ratio; LMWH, low molecular weight heparin; NOAC, new anticoagulants; OC, oral contraceptives; SSRI, selective serotonin reuptake inhibitors; and UFH, unfractionated heparin.

PRÉVENTION SECONDAIRE

- Risque faible: HBPM premier trimestre puis ASA 80*
- Risque élevé: HBPM premier trim. puis warfarine
- Pte sous DOAC : cesser DOAC puis HBPM suivi de warfarine
    - Pte sous AP : ASA
    - Pte anticoagulée: stop DOAC ou coumadin puis…

<u>Contraceptif oraux post AVC</u> :

oestrogènes : non

progestatif seuls: oui plus que non

post dissection traumatique :??..

Stérilet a considérer

Traitements Antithrombotiques durant la grossesse

Guidelines

International Journal of Stroke WSO

Canadian stroke best practice consensus statement: Secondary stroke prevention during pregnancy

Richard H Swartz[1,2], Noor Niyar N Ladhani[1,3], Norine Foley[4,5], Kara Nerenberg[6], Simerpreet Bal[7], Jon Barrett[1,3], Cheryl Bushnell[8], Wee-Shian Chan[9], Radha Chari[10], Dariush Dowlatshahi[11], Meryem El Amrani[12], Shital Gandhi[3,13], Gord Gubitz[14,15], Michael D Hill[7,16], Andra James[17], Thomas Jeerakathil[18], Albert Jin[19], Adam Kirton[7,16], Sylvain Lanthier[12], Andrea Lausman[3,20], Lisa Rae Leffert[21], Jennifer Mandzia[22], Bijoy Menon[7,16], Aleksandra Pikula[2,23], Alexandre Poppe[24], Jayson Potts[9], Joel Ray[3,20], Gustavo Saposnik[2,25], Mukul Sharma[26], Eric E Smith[7,16], Sanjit Bhogal[5], Elisabeth Smitko[27] and M Patrice Lindsay[27,28]; on behalf of the Heart and Stroke Foundation Canadian Stroke Best Practice Advisory Committees

International Journal of Stroke
2018, Vol. 13(4) 406–419

DOI: 10.1177/1747493017743801
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2A. Antithrombotic Use in Pregnancy (Antiplatelets and Anticoagulants) Following Ischemic Stroke or Transient Ischemic Attack (TIA)

i. Decision-making regarding antithrombotic use can be complex and a multidisciplinary review may be needed to assess maternal and fetal risk/benefit of the options.
   a. Antithrombotic management decisions can be tailored on an individual basis and may be informed by many issues, such as:
      - stroke etiology and accompanying stroke recurrence risk outside of pregnancy (e.g. prosthetic heart valve vs. cryptogenic stroke);
      - the size and recency of the stroke (e.g. bleeding risk is higher with larger and more recent infarcts);
      - the stage of pregnancy (e.g. peripartum and post-partum stroke risk is higher than first and second trimester).
   b. If considering anticoagulation, in addition to factors listed above, consider a woman's medical and obstetrical history. For example, a woman with a history of preterm labor or rapid delivery can be at higher risk of an early or rapid delivery, making a planned cessation of LMWH more challenging.

ii. In some women with a prior ischemic stroke whose underlying mechanism of stroke has resolved and residual risk is presumed to be comparable to the general population and who are not already on antithrombotics, it is reasonable to consider not starting antithrombotic prophylaxis during pregnancy.

iii. If antiplatelet agents (clopidogrel, acetylsalicylic acid, combined acetylsalicylic acid and extended-release dipyridamole, or ticagrelor at any dose at any dose) are indicated or already in use for stroke prevention, changing to low-dose acetylsalicylic acid (81 mg daily) is preferred prior to pregnancy or once a pregnancy is confirmed.
   a. There is insufficient evidence to support the safety of antiplatelet agents other than acetylsalicylic acid in pregnancy. However, there may be cases where other antiplatelet agents are clinically indicated and these situations should be addressed on a case-by-case basis (e.g. Clopidogrel in the setting of coronary stents).
   b. In women for whom antiplatelet agents would be recommended for stroke prevention, low dose acetylsalicylic acid is reasonable pre-conception, first trimester and throughout the rest of pregnancy.

Note: Non-Steroidal Anti-Inflamatory Drugs (NSAIDs) have been linked to premature closure of the ductus arteriosis when used in the third trimester and may impair fetal renal function. Low-dose ASA, while an NSAID, has not been reported to increase the risk of premature closure of the ductus arteriosis in clinical trials, and increases in fetal renal impairment have not been reported. Other guidelines[38] acknowledge case control studies that associated increased risk of fetal gastroschisis with ASA taken before the eleventh week of pregnancy. Results from more recent RCTs including EAGeR[29] and ASPRE,[31] using

i)Décision de donner antithrombotique et lequel est complexe et necessite discussion multidisciplinaire

ii) Si le mécanisme de l'AVC est résolu et que la patien te ne prend plus d'antithrombotique , considérer ne pas en commencer durant la grossesse

ii)

1. Si la pte est sous antiplaquettaire changer pour ASA avant la grossesse
2. Pas de données pour clopidogrel

3. **ASA est raisonnable pré-conception, premier trimestre et reste de la grossesse**

Le **gastroschisis**, aussi appelé laparoschisis, est une malformation congénitale de la paroi abdominale qui consiste en une fermeture incomplète de celle-ci, créant une fente qui laisse sortir une partie des intestins flottant dans le liquide amniotique.

low-dose ASA pre-conception (81 mg) or after 11 weeks (150 mg) to reduce the risks of pregnancy loss or the development of preeclampsia, have not been associated with increased risk of major adverse events when used throughout pregnancy.

c. Low-dose ASA can be considered during breastfeeding since there is evidence that aspirin is not excreted into breast milk and salicylate levels are low in women taking daily low-dose aspirin. Higher dose of daily aspirin may have additional risks, with possible risks of metabolic acidosis and theoretical risks of Reye's syndrome in infants exposed to high doses of salicylic acid.[39–41]

iv. Warfarin is potentially teratogenic and should be avoided, especially between 6 and 12 weeks gestational age. When anticoagulation is considered, low molecular weight heparin (LMWH) is preferred throughout pregnancy.
   a. In certain rare situations with very strong indications for warfarin (e.g. women with a mechanical cardiac valve), collaboration with thrombosis experts may be required. In these situations, switching to an alternative to warfarin may be considered as soon as pregnancy is discovered, and could consider restarting warfarin after the twelfth week of pregnancy until closer to delivery. Multidisciplinary management of these situations is preferred.

v. There are insufficient data on the safety of direct oral anticoagulants (DOAC) (apixaban, dabigatran, edoxaban, rivaroxaban) in pregnancy. Switching to LMWH is encouraged as soon as a pregnancy is identified or if pregnancy is planned.

vi. In certain circumstances, therapeutic doses of LMWH can be considered a reasonable alternative to ASA or prophylactic doses could be considered with or without low-dose ASA. For example:
   a. A woman considered at high stroke/thrombotic risk (e.g. with multiple strokes),
   b. A woman with known hypercoagulability (e.g. anti-phospholipid antibody syndrome).

vii. Low-dose LMWH should be stopped at least 12 hours prior to administration of regional anesthesia, and full-dose LMWH should be stopped at least 24 hours in advance of regional anesthesia or planned induction.[7]

viii. Intravenous unfractionated heparin could be considered in a hospitalized woman in place of LMWH, using standardized local protocols, especially if there is concern about need for urgent delivery or invasive procedures.
   a. When using IV unfractionated heparin, a low dose, acute coronary syndrome nomogram, without bolus, is preferred in stroke patients, and would also be preferred in pregnancy.

ix. LMWH or unfractionated heparin can be restarted at least 4 to 6 hours after the removal of the neuraxial catheter if bleeding is well controlled and there are no neuraxial concerns, and continued for 6–12 weeks post-delivery.

x. After 6 to 12 weeks post-delivery, consider the choice of antithrombotic that was recommended outside of pregnancy, taking into account issues regarding breastfeeding (see section C above for links), and future pregnancy planning.
   a. If anticoagulation is required, low molecular weight heparin and warfarin are both considered safe options during breastfeeding. The safety of direct oral anticoagulants in breastfeeding has not been established.

- ASA : ok durant l'allaitement à petite dose
- Warfarin : éviter sem 6-12
- DOAC: changer pour HBPM..
- HBPM: haut risque ex: APL
- HBPM ou warfarin: sécuritaire durant l'allaitement
- DOAC: pas de données durant l'allaitement

2C. Statins for Ischemic Stroke Prevention in Pregnancy

i. Interpretation of lipid levels is unreliable in pregnancy due to the normal physiologic changes of pregnancy and should not be used to guide decisions about therapy. In addition, serum lipid levels should not be routinely measured during pregnancy. First-line management of dyslipidemia includes counseling for healthy diet and exercise.

ii. There is insufficient evidence regarding the safety of statins in pregnancy and lactation. It is reasonable to temporarily interrupt statin therapy preconception and throughout pregnancy.

iii. The timing for restarting, or newly prescribing, statins for secondary stroke prevention after delivery should be individualized based on specific clinical circumstances (e.g. presence of high-risk conditions such as recent MI, compatibility with breastfeeding plans).

CONCLUSIONS

- La période le plus à risque pour les AVC est le <u>péri et post-partum immédiat</u>

- La **thrombolyse IV:** n'est pas contre - indiquée
- La **thrombectomie mécanique:** n'est pas contre - indiquée

- Si la patiente est une candidate évidente à la thrombectomie mécanique
  - ex: Gros NIH et ACM hyperdense au CT simple

Considérer

- <u>Ne pas faire d'angioscan</u> (si ACM hyperdense et clinique d'AVC majeur) - <u>Ne pas donner TPA IV</u> (si va en thrombectomie)

- Patiente enceinte avec **<u>céphalée aiguë</u>**: soyez vigilants

- Patiente sous <u>Antiplaquettaires</u>: garder ASA ou changer pour ASA 80 durant toute la grossesse
- Patiente <u>Anticoagulée</u>: cesser DOAC ou warfarine: HBPM 1er trimestre puis warfarine

- Idéalement pas de CO post AVC; considérer progestatifs seuls, stérilet

extras

29. Schisterman EF, Silver RM, Lesher LL, et al. Preconception low-dose aspirin and pregnancy outcomes: Results from the EAGeR randomised trial. *Lancet* 2014; 384: 29–36.

31. Rolnik DL, Wright D, Poon LC, et al. Aspirin versus placebo in pregnancies at high risk for preterm pre-eclampsia. *N Engl J Med* 2017; 377: 613–622.

Conditions associées à la **pré-éclampsie** (HTA + protéinurie)

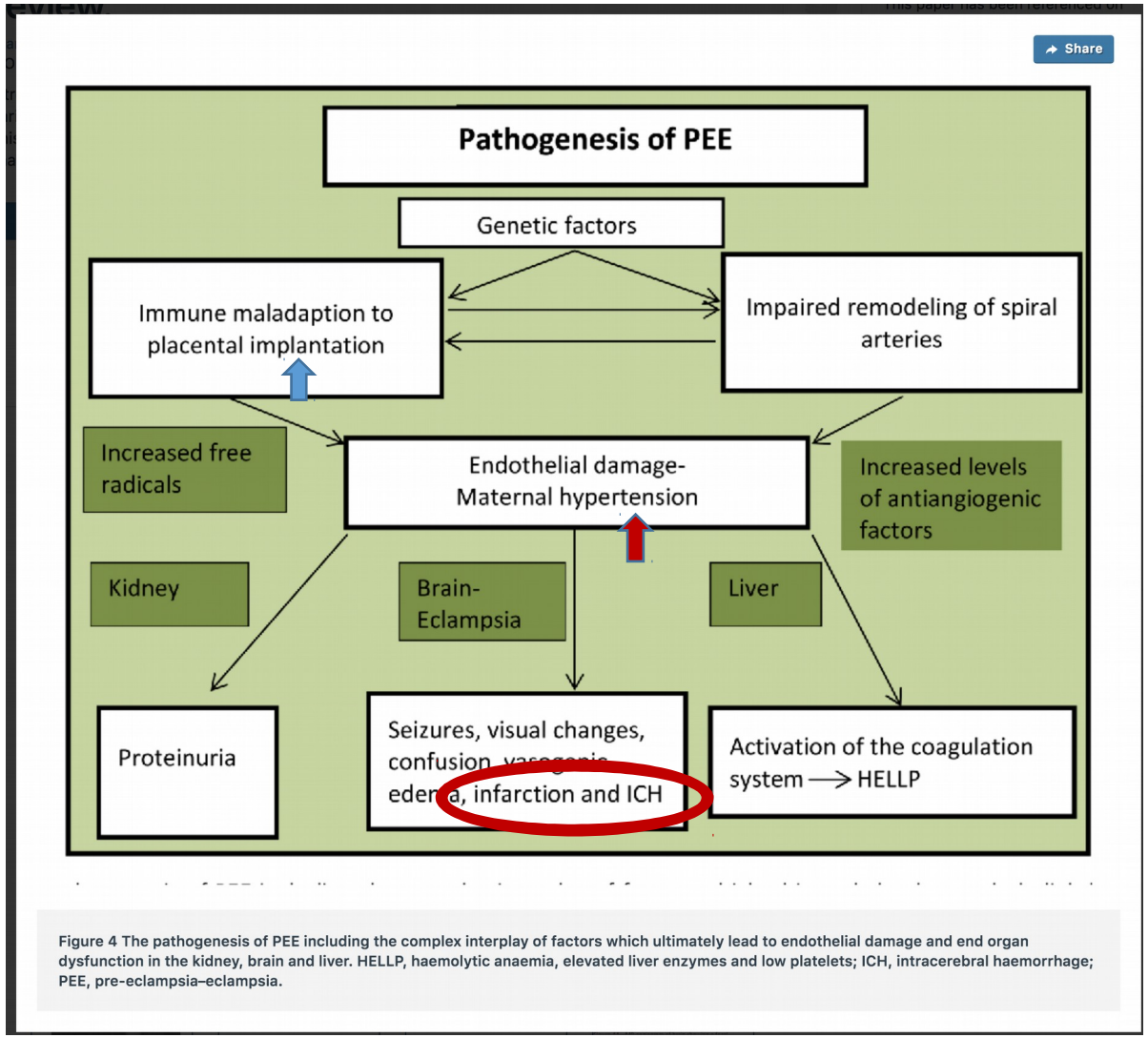

Figure 4 The pathogenesis of PEE including the complex interplay of factors which ultimately lead to endothelial damage and end organ dysfunction in the kidney, brain and liver. HELLP, haemolytic anaemia, elevated liver enzymes and low platelets; ICH, intracerebral haemorrhage; PEE, pre-eclampsia–eclampsia.

O'Neal MA, Feske SK. Stroke in pregnancy: a case-oriented review. *Practical Neurology* 2016;**16**:23-34.

- Pré-éclampsie associée à une interaction complexe entre
  - Facteurs génétiques
  - Facteurs immuns
  - Facteurs vasculaires
    - Remodeling
    - Dommage endothélial

- Serait déclenché par une <u>implantation anormale du placenta</u>
- L'ischémie placentaire résultante conduirait à un débalancement entre les facteurs pro angiogéniques et anti angiogéniques et une réponse vasoconstrictive exagérée conduisant à <u>dysfonction endothéliale</u>, hyperaggregation plaquettaire et **HTA**