Letter to the Editor: Aspirin resistance and adverse pregnancy outcomes

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To the Editor,

We read with great interest the article by Wójtowicz *et al.* who found an association between aspirin resistance, defined by a high level of urinary 11-dehydrothromboxane B_2, and adverse pregnancy outcomes, including preeclampsia and small-for-gestational-age (SGA) newborns in women taking 75 mg of aspirin daily (Wojtowicz *et al.* 2011). Their data strengthen the observations of Dumont *et al.* who showed that the efficacy of aspirin in preventing adverse pregnancy outcomes was optimal when bleeding time was ≥2 min 10 days after treatment was started (Dumont *et al.* 1999). Their results are also in agreement with those of Caron *et al.* who determined, with a platelet function analyzer (PFA-100), that approximately 30% of women are resistant to 81 mg of daily aspirin in early pregnancy (Caron *et al.* 2009).

The converging findings of these three studies could have a huge impact on women's health in future. While the hypothesis that low-dose aspirin might prevent preeclampsia held considerable interest in the last three decades, it was just recently that meta-analyses demonstrated that its effectiveness was optimized when initiated before 16 weeks' gestation, before physiological spiral artery transformation was mostly completed (Bujold *et al.* 2009; Bujold *et al.* 2010). Therefore, since several experts and clinicians are now recommending early administration of low-dose aspirin, usually from 75 to 100 mg daily, for the preclusion of preeclampsia in high-risk women, these studies indicate that the dosage could be insufficient in up to one-third of them. More importantly, they suggested that at-risk women could be identified early in pregnancy and that higher aspirin dosage could help to avert adverse pregnancy outcomes, including preeclampsia, SGA and even preterm birth.

If these hypotheses are confirmed, it would mean that potentially more than half of recurrent

preeclampsia cases, and mainly severe preeclampsia, could be avoided. Preeclampsia, a leading cause of maternal morbidity and mortality worldwide, is associated with more than 50,000 maternal deaths every year in developing countries. Facing this growing body of evidence that low-dose aspirin offers potential benefits in selected pregnancies, it is becoming mandatory and urgent to perform randomized trials that will aim to specify the most favourable aspirin dosage, ultimately maximizing the prevention of adverse pregnancy outcomes in at-risk women, while minimizing potential side-effects related to aspirin. Once these studies are carried out, individualized specific aspirin dosages for minimal resistance and optimal prevention could be recommended.

REFERENCES

1 Bujold E, Morency AM, Roberge S, Lacasse Y, Forest JC, Giguere Y (2009) Acetylsalicylic acid for the prevention of preeclampsia and intra-uterine growth restriction in women with abnormal uterine artery Doppler: a systematic review and meta-analysis. J Obstet Gynaecol Can **31**: 818-826.
2 Bujold E, Roberge S, Lacasse Y, Bureau M, Audibert F, Marcoux S et al. (2010) Prevention of preeclampsia and intrauterine growth restriction with aspirin started in early pregnancy: a meta-analysis. Obstet Gynecol **116**: 402-414.
3 Caron N, Rivard GE, Michon N, Morin F, Pilon D, Moutquin JM, Rey E (2009) Low-dose ASA response using the PFA-100 in women with high-risk pregnancy. J Obstet Gynaecol Can **31**: 1022-1027.
4 Dumont A, Flahault A, Beaufils M, Verdy E, Uzan S (1999) Effect of aspirin in pregnant women is dependent on increase in bleeding time. Am J Obstet Gynecol **180**: 135-140.
5 Wójtowicz A, Undas A, Huras H, Musiał J, Rytlewski K, Reroń A, Wilczak M, Jach R (2011) Aspirin resistance may be associated with adverse pregnancy outcomes. Neuro Endocrinol Lett **32**(3): 334-9.