



# Motherisk Update

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## Multivitamin supplements for pregnant women *New insights*

### ABSTRACT

**QUESTION** One of my patients is planning pregnancy and has started taking multivitamin supplements. She is experiencing gastric discomfort. What are the alternatives?

**ANSWER** Gastric discomfort is usually related to iron intake; pregnant women could use supplements with less iron. Pregnant women need 0.4 to 1.0 mg of folic acid daily. If they have a family history of neural tube defects (NTDs), insulin-dependent diabetes mellitus, or epilepsy, or are currently taking valproic acid, carbamazepine, or antifolates (eg, sulfonamides), they are at intermediate-to-high risk of having babies with NTDs and need 4.0 to 5.0 mg of folic acid daily.

### RÉSUMÉ

**QUESTION** L'une de mes patientes planifie une grossesse et a commencé à prendre des suppléments de multivitamines. Elle souffre depuis ce temps de malaises gastriques. Quelles sont les options de rechange?

**RÉPONSE** Les malaises gastriques sont souvent attribuables à l'ingestion de fer; les femmes enceintes peuvent prendre des suppléments contenant moins de fer. Les femmes enceintes ont besoin de prendre de 0,4 à 1,0 mg d'acide folique par jour. Si elles ont des antécédents familiaux d'anomalies du tube neural, de diabète insulino-dépendant ou d'épilepsie, ou si elles prennent actuellement de l'acide valproïque, de la carbamazépine, des antifoliques (par ex. des sulfonamides), elles courent des risques allant de modérés à élevés d'avoir un enfant souffrant d'anomalies du tube neural et doivent prendre de 4,0 à 5,0 mg d'acide folique par jour.

Prenatal multivitamins are recommended before and during pregnancy to prevent iron-deficiency anemia and neural tube defects (NTDs).<sup>1-3</sup> A range of prenatal supplements are available; most meet the required dietary allowance for pregnant women.

Some patients have very low tolerance of iron because they have morning sickness, which is experienced by 50% to 80% of pregnant women.<sup>4</sup> A new twice-a-day prenatal multivitamin supplement (PregVit<sup>®</sup>) might be an appropriate alternative for women unable to tolerate the side effects of ingesting iron at high doses. The morning tablet contains

35 mg of iron, almost 50% less than is in most prenatal multivitamins. Calcium is provided in the night tablet so that it does not interfere with the absorption of iron, which is why the lower dose of iron is adequate.<sup>5,6</sup> A recent study at the Motherisk program showed that patients absorbed similar amounts of iron from PregVit<sup>®</sup> and another widely used prenatal supplement.

Even today, following folate fortification of flour, about half of Canadian women have folate levels below the protective 900 nM and thus are at increased risk of having babies with NTDs.<sup>7</sup> Folic acid supplementation is especially important before

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closure of the neural tube at approximately 28 days' gestation (iron becomes more important during the second and third trimesters). Folic acid might be beneficial throughout the first trimester in preventing other malformations also.<sup>8</sup>

Women who have a family history of NTDs, insulin-dependent diabetes mellitus, or epilepsy, or are currently taking valproic acid, carbamazepine, or antifolates (eg, sulfonamides) are at intermediate-to-high risk of having babies with NTDs. These women need 4 mg to 5 mg of folic acid daily starting before they become pregnant.

New and potentially important findings were recently reported in an analysis of all published folic acid dose-level studies. Results demonstrated that to achieve the needed serum concentration of 900 nM, 5 mg of folic acid are required daily. This dose, rather than the previously recommended 0.4 to 1.0 mg dose, could prevent 85% of folate-dependent NTDs.<sup>9</sup> The main concern with this high dose of folic acid is that it could mask vitamin B<sub>12</sub>-deficiency pernicious anemia. Making a general recommendation for higher folate supplementation must await in-depth analysis of the effects of the "low folate" fortification instituted in the United States and Canada in 1997-1998.

Finally, prenatal multivitamins contain iron and calcium, both of which are potent inhibitors of absorption of levothyroxine.<sup>10,11</sup> A recent study found that doses of levothyroxine do not need to be modified if prenatal multivitamins are taken 4 hours after ingestion of levothyroxine.<sup>12</sup> Concomitant ingestion of iron causes marked decreases in the bioavailability of a variety of drugs (Table 1).<sup>13</sup> The major mechanism of these drug interactions is the formation of iron-drug complexes. ❁

### References

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**Table 1. Drugs with decreased bioavailability when taken concomitantly with iron**

Captopril
Carbidopa, levodopa, and methyldopa
Ciprofloxacin
Folic acid
Levothyroxine
Penicillamine
Tetracycline
Tetracycline derivatives (doxycycline, methacycline, and oxytetracycline)

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## MOTHERISK

Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. Dr Nava-Ocampo and Dr Soldin are members and Dr Koren is Director of the Motherisk Program. Dr Koren, a Senior Scientist at the Canadian Institutes for Health Research, is supported by the Research Leadership for Better Pharmacotherapy during Pregnancy and Lactation and, in part, by a grant from the Canadian Institutes for Health Research.

Do you have questions about the safety of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the Motherisk Program by fax at (416) 813-7562; they will be addressed in future Motherisk Updates.

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