

GUIDELINES & PROTOCOLS

ADVISORY COMMITTEE

Folate Deficiency - Investigation & Management

Effective Date: January 1, 2012

BASICS

Introduction

Folate deficiency is associated with megaloblastic anemia and birth defects (especially neural tube defects).¹ Folate and folic acid are forms of a water-soluble B vitamin. Folate occurs naturally in food, and folic acid is the synthetic form of this vitamin. Folate is found in vegetables, fruit, cereals, and dairy products (See Appendix A - *Dietary sources of folate*).²

The average folate levels have increased significantly in the population, and folate deficiency is now rare. In two outpatient laboratories in British Columbia, 99.8% and 99.1% of folate tests were normal in 2010.³

Serum folate and red blood cell (RBC) folate tests are no longer being offered (except at Vancouver General Hospital and St. Paul's hospital under limited indications and require approval from the respective Medical Biochemist on call).

Scope

This guideline covers the investigation and management of folate deficiency in adults (≥ 19 years).

Diagnostic code: 281.2

Risk Factors

The prevalence of folate deficiency has markedly decreased since Canada introduced mandatory fortification of flour and pasta by folic acid. However, some individuals remain at risk for folate deficiency (see below).¹

Prevention:

It is recommended that all women planning a pregnancy take a daily supplement containing folic acid to reduce the risk of neural tube defects:²

- Patients with no personal health risks, planned pregnancy, and good compliance: a good diet of folate-rich foods and daily supplementation with a multivitamin with folic acid (0.4–1.0 mg) for at least two to three months before conception and throughout pregnancy and the postpartum period (4–6 weeks) or as long as breastfeeding continues.
- Patients with health risks, including epilepsy, insulin dependent diabetes, obesity with BMI >35 kg/m², family history of neural tube defects, belonging to a high-risk ethnic group (e.g., Indian ancestry): increased dietary intake of folate-rich foods and daily supplementation with multivitamins with 5 mg folic acid beginning at least three months before conception and continuing until 10 to 12 weeks post conception. Daily supplementation with a multivitamin containing 0.4–1 mg of folic acid should continue from then on, throughout pregnancy and the postpartum period (4–6 weeks), or as long as breast feeding continues.

DIAGNOSIS

Folate deficiency may be suspected in patients with macrocytic anemia and/or hypersegmented neutrophils, in alcoholics, in those with dietary deficiency or malabsorption, during high demand periods like pregnancy and perinatal period, and in patients taking certain medications such as methotrexate, oral contraceptives, phenytoin, pyrimethamine, sulfasalazine, and trimethoprim.^{4,5}



Ministry of
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MANAGEMENT

Treatment

If folate deficiency is suspected, it is reasonable to give oral folic acid (0.4-1 mg/day) without doing laboratory investigation for deficiency at least until the hemoglobin and mean corpuscular volume normalizes (or longer if the underlying cause cannot be eliminated).

CAUTION: In suspected cobalamin deficiency, both cobalamin and folate should be supplemented, as folic acid alone may exacerbate/precipitate neurological symptoms.

Supplements

- Folic acid in doses usually used in supplementation [as described above] is generally non-toxic/not associated with serious harms.^{5, 6} Consider supplementation when on medications, e.g., methotrexate.⁷
- Over the counter products include: 0.4 mg and 1 mg tablets.*
- PharmaCare coverage: Prescription products include: 5 mg tablets; some PharmaCare plans provide coverage.**

*Only strengths and formulations generally used for prevention and/or treatment of folic acid deficiency are listed

**Coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles. See www.health.gov.bc.ca/pharmacare/ and www.health.gov.bc.ca/pharmacare/benefitslookup/ for more information.

Note: For complete details, please review product monographs at webprod.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp and regularly review current Health Canada advisories, warnings and recalls at: www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html for the most up to date information.

RESOURCES

References

1. Wilson RD, Désilets V, Wyatt P, Langlois S, Gagnon A, Allen V, Blight C, Johnson J, Audibert F, Brock J, Koren G, Goh I, Nguyen P, Kapur B. Preconceptual vitamin / folic acid supplementation 2007: The Use of Folic Acid in Combination with a Multivitamin Supplement for the Prevention of Neural Tube Defects and Other Congenital Anomalies. Joint SOGC-MOTHERISK Clinical practice guideline. *J Obstet Gynaecol Can.* 2007;29:1003-13.
2. Office of Dietary Supplements. National Institutes of Health. Dietary Supplement Fact Sheet: Folate; Updated 4/15/2009. Available from: <http://ods.od.nih.gov/factsheets/Folate-HealthProfessional/>. Verified on 2011 August 08.
3. Dalal B, RCPSC-General Pathology, 2010, personal communication.
4. Allen LH. Causes of vitamin B12 and folate deficiency. *Food Nutr Bull.* 2008;29:S20-34.
5. 5. e-CPS: Folic Acid monograph; Canadian Pharmacy Association; accessed June 29th 2011: www.e-therapeutics.ca/cps/showMonograph.action?simpleMonographID=m223400
6. Clinical Guidelines: Folic Acid for the Prevention of Neural Tube Defects: US Preventative Services Task Force Recommendation Statement: *Ann Intern Med* 2009;150:626-531
7. Ortiz Z, Shea B, Suarez-Almazor ME, et al., Folic acid and Folinic acid for reducing side effects in patients receiving methotrexate for rheumatoid arthritis (Review). *Cochrane Database of Systematic Reviews* 1999, Issue 4. Art. No.: CD000951.

Abbreviations

BMI – body mass index

Appendices

Appendix A – Dietary sources of folate

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association and adopted by the Medical Services Commission.

A mobile version of this and other guidelines is also available at www.BCGuidelines.ca

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

Contact Information

Guidelines and Protocols Advisory Committee
PO Box 9642 STN PROV GOVT
Victoria BC V8W 9P1
E-mail: hth.guidelines@gov.bc.ca
Web site: www.BCGuidelines.ca

DISCLAIMER

The Clinical Practice Guidelines (the "Guidelines") have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problems. **We cannot respond to patients or patient advocates requesting advice on issues related to medical conditions. If you need medical advice, please contact a health care professional.**

Appendix A: Dietary sources of folate

Dietary Sources of Folate ¹ (RDA* 0.4mg, pregnant women 0.6mg)	
Food	milligrams
Ready-to-eat cereal, fortified, 1 serving	0.4
Potato, Baked, flesh and skin, 1 medium	0.7
Banana, raw, 1	0.68
Garbanzo beans, 4 oz	0.57
Chicken breast, ½ breast	0.52
Oatmeal, instant, fortified, 1 packet	0.42
Pork loin, lean, 3 oz	0.42
Roast beef, lean, 3 oz	0.32
Trout, rainbow, 3 oz	0.29
Sunflower seeds, 1 oz	0.23
Spinach, 8 oz	0.14
Tomato juice, 6 oz	0.2
Avocado, 8 oz	0.2
Salmon, Sockeye, 3 oz	0.19
Tuna, 3 oz	0.18
Wheat bran, 4 oz	0.18
Peanut butter, 2 Tbs.	0.15
Walnuts, 1 oz	0.15
Soybeans, green, 8 oz	0.05
Lima beans, 8 oz	0.1

¹Office of Dietary Supplements. National Institutes of Health. Dietary Supplement Fact Sheet: Folate; Updated 4/15/2009. Available from: <http://ods.od.nih.gov/factsheets/Folate-HealthProfessional/>.

*Recommended dietary allowance