Medical Biochemistry

Seven Things Clinicians and Patients Should Question

by
Canadian Association of Medical Biochemists

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Choosing Wisely Canada™
In collaboration with the Canadian Medical Association

1 **Don't order serum folate testing in the absence of the following: anemia with red blood cell macrocytes or hypersegmented polynuclear neutrophils *and* a reasonable clinical suspicion of a nutritional deficiency such as an unsupplemented restrictive diet, severe Alcohol Use Disorder, or malabsorption.**

Since 1998, all wheat white flours for food use sold in Canada and United States are enriched with folic acid as a mandatory legal requirement. The main reason for this supplementation is to prevent neural tube defects in newborns. Folates are found in processed food that contains white flour and in green leafy vegetables, legumes, some fruits and beans. Folate deficiency is therefore now encountered very rarely in Canada.

For most patients at risk for folate deficiency, like those with malabsorption, it is more practical and economical to treat with multivitamin supplements including folic acid, than to test for deficiency. The Society of Obstetricians and Gynecologists of Canada recommends universal supplementation for women in the reproductive age group. Investigations are not required prior to initiating folic acid in women considering pregnancy.

2 **Don't order an erythrocyte sedimentation rate (ESR) to screen asymptomatic patients or as a general test to look for inflammation in patients with undiagnosed conditions.**

ESR is a non-specific inflammation marker influenced by various factors including anemia, pregnancy, and smoking. C-reactive protein (CRP) is a less expensive and more sensitive and specific reflection of the acute phase of inflammation, hence should be used for this purpose. In the first 24 hours of a disease process, the CRP will be elevated, while the ESR may be normal. If the source of inflammation is removed, CRP will normalize within a day or so, while ESR will remain elevated for days. Only CRP should be used as a measure of systemic inflammation.

3 **Don't order amylase in addition to lipase to detect pancreatitis.**

In pancreatitis, levels of amylase and lipase have been found to correlate very well. However, multiple studies have shown that lipase is a more sensitive and specific marker of acute pancreatitis than amylase. Moreover, lipase stays elevated longer than amylase, which is useful in cases of delayed presentation. However, false negative results may still be observed after many days, but amylase is not helpful in those cases. For children, pediatric specific reference ranges should be adapted.

4 **Don't request a serum protein electrophoresis in asymptomatic patients in the absence of otherwise unexplained hypercalcemia, renal insufficiency, anemia or lytic bone lesions.**

Serum protein electrophoresis (SPE) is mainly indicated to detect monoclonal gammopathy in patients who have clinical symptoms and signs related to multiple myeloma, amyloidosis, or Waldenstrom macroglobulinemia. It may also be performed in certain uncommon diseases associated with a monoclonal protein like POEMS syndrome and some forms of polyneuropathy.

About 3% of the population above the age of 50, have a monoclonal gammopathy of undetermined significance (MGUS). Current practice guidelines do not recommend routine screening for MGUS in the general population because of the lack of proven benefit, absence of actionable preventive therapy and creation of unnecessary anxiety for some patients.

SPE is not a sensitive test to detect inflammation, C-reactive protein is a better and less costly alternative that is more responsive to changes in the patient status.

5 Don't request uric acid as part of the routine evaluation of cardiovascular risk, obesity or diabetes.

Although evidence of a causative link between hyperuricemia and cardiometabolic risk is mounting, it still does not support the use of pharmacotherapy and its concentration is not used in equations for estimating vascular risk. Asymptomatic hyperuricemia is a frequent, coincidental, biochemical finding that does not require any treatment.

Uric acid should not be measured routinely, but its measurement may be considered mainly in the following situations:

- Investigation of acute joint pain
- Follow-up of hypouricemic treatment
- Follow-up of patients with kidney disease and kidney stone disease
- Preeclampsia
- Tumor lysis syndrome

6 Don't order serum total bile acids to assess cholestasis in non-pregnant women and general populations.

Serum total bile acids tests (TBA) are used primarily for the evaluation and monitoring of intrahepatic cholestasis of pregnancy (ICP), a condition affecting 1-2% of pregnant women in North America. ICP is associated with an increased risk of perinatal complications including premature birth, intrauterine asphyxia, fetal bradycardia and even stillbirth. Severe ICP is defined when serum TBA is above 40 umol/L, and the likelihood of stillbirth is significantly increased when the serum TBA concentration is >100mmol/L, which makes it a good prognostic marker. However, in non-pregnant individuals with suspected cholestasis, TBA is not an effective test to assess liver dysfunction compared to traditional liver panel tests (e.g., bilirubin, albumin, ALT, GGT and ALP). In the context of familial intrahepatic cholestasis, the serum TBA is considered as a tier 2 investigation which is ordered by pediatric gastroenterologists only. The urine bile acids profile is the appropriate test for the investigation of disorders of bile acid synthesis, not serum TBA.

7 Don't order copper and ceruloplasmin as routine screening tests for children with global developmental delay/intellectual disability.

Global developmental delay and intellectual disability (GDD/ID) affect 3% of the paediatric population. Since its differential diagnosis is broad, community –based clinicians tend to order copper and ceruloplasmin tests to screen for Wilson's and Menkes disease (mutations in ATP7A or ATP7B). However, a recent study determined that neither Wilson's nor Menkes disease have been identified using these tests in children with global developmental delay/intellectual disability. In addition, false abnormal copper and ceruloplasmin results lead to an increase in the number of total referrals and unnecessary follow ups (4% in the above study). Children with Wilson's disease are more likely to present with hepatic manifestations than neurologic symptoms, while those with Menkes disease show multiple abnormalities including developmental delay and epilepsy typically within the first 3 months of life.

How the list was created

The list was developed under the guidance of a committee formed with the specific intent of producing a list of 5 recommendations. All CAMB members were invited to participate and members were nominated by the CAMB board executive. The committee members reviewed the CWC guidance on producing recommendations and put forward a number of topics that were refined in discussion during committee meetings. A preliminary list of 22 topics was produced by the committee. A survey of all the membership was conducted by an electronic survey with options to add more suggestions. The ranked result of the survey was discussed with the committee and duplicate results were not considered. Weighting of each topic was reviewed and a list of 5 topics was agreed upon.

Recommendations 6 & 7 were approved by the executive board of the Canadian Association of Medical Biochemists (CAMB) in May 2022. These recommendations were further revised by the CAMB Choosing Wisely Canada committee in September 2022. Additionally, a rapid literature review to confirm recommendation 7 was conducted by CADTH in December 2022. The final English version of the recommendations as well as their French translations were approved by all the CAMB members in March 2023.

Sources

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About the Canadian Association of Medical Biochemists

The CAMB is the national association that represents physicians specialized in medical biochemistry, a specialty recognized by the Royal College of Physicians and Surgeons of Canada. Medical Biochemists directs clinical laboratories, consults, diagnoses and treats patients with a variety of metabolic disorders and biochemical abnormalities. The CAMB promotes quality and security in laboratory medicine and in the clinical use of laboratory information through education, research, and clinical practice. The CAMB aims to serve and educate the public and also to enhance career opportunities of its members through continuous professional development and advocacy initiatives.

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About Choosing Wisely Canada

Choosing Wisely Canada is the national voice for reducing unnecessary tests and treatments in health care. One of its important functions is to help clinicians and patients engage in conversations that lead to smart and effective care choices.

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