

# Omega-3 Fatty Acids and Their Role in Coronary Heart Disease Prevention

It has long been recognized that Japanese populations exhibit a significantly lower rate of death from acute myocardial infarction (AMI) than North Americans, despite only moderate differences in cholesterol levels. Similar reductions in AMI, as well as ischemic heart disease and atherosclerosis, have been seen in other populations with a high intake of fish in the diet.

The beneficial effects of diet, as seen in the fish-eating sectors, are attributed to the large amounts of the omega-3 fatty acids known as eicosapentaenoic acid, 20:5n-3 (EPA) and docosahexaenoic acid, 22:6n-3 (DHA).<sup>1</sup>

Epidemiological and controlled clinical trials have indicated that omega-3 fatty acids from fish and fish oils (EPA/DHA) play a significant role in the prevention and supportive management of coronary heart disease. Various mechanisms for the cardioprotective effects of EPA/DHA have been proposed including anti-arrhythmic, anti-thrombotic, improved endothelial relaxation and triglyceride-lowering.<sup>1</sup>

## DIAGNOSTIC TESTING

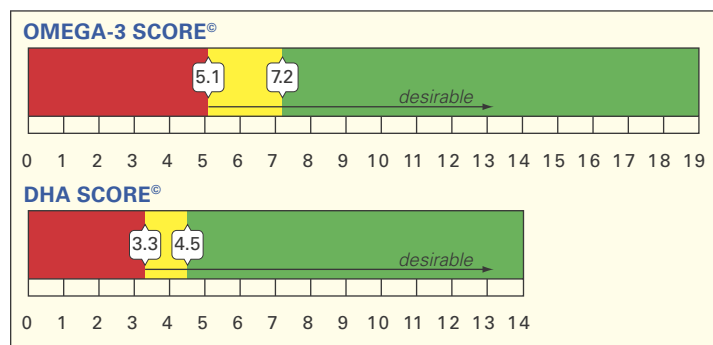
The vast majority of North Americans will exhibit relatively low levels of total omega-3 fatty acids in their plasma. This low physiological status usually reflects the very low intakes of EPA/DHA in a typical North America diet (100–150 mg of EPA/DHA combined/day). However, different sources of EPA/DHA from fish, fish oil supplements, or 'novel' foods containing unusually high levels of EPA/DHA can be expected to markedly improve the total omega-3 and DHA status in the body within 6-8 weeks if they are consumed on a regular basis.

Fatty acid analysis of serum (or plasma) phospholipid is a useful biomarker for assessing nutritional status and EPA/DHA intakes in relation to potential risk.<sup>3,4</sup> These analyses and the reporting format as the 'Omega-3 Score' and the 'DHA Score' use methods provided by Nutrasource Diagnostics Inc., a company originating from the University of Guelph.

The value of carrying out the assays, 1) as a baseline and 2) after 6-8 weeks of diet modification or supplementation, is to monitor for variation in digestibility and bioavailability, as well as compliance with supplementation and to ensure attainment of targeted blood levels.

**Note:** MDS provides national access to the Omega-3: Fatty Acid Profile. This test is not covered by provincial health plans but may be covered by a patient's private insurance plan. Patients will be charged at the time of specimen collection and should submit their receipt to their insurance plan.

Sample Report:



## DIETARY RECOMMENDATIONS

The levels of the long-chain omega-3 fatty acids can best be increased in the body tissues (blood, platelets, heart etc.) via their direct consumption and suitable sources are detailed in Table 1.<sup>1</sup>

**TABLE I**  
**OMEGA-3 FATTY ACID CONTENT OF SELECTED FOODS AND SUPPLEMENTS**

Product	Concentration of sum of EPA and DHA
Fish or Seafood	
Mackerel	2500mg/100g
Herring	1700mg/100g
Salmon	1200mg/100g
Tuna	400mg/100g
Shrimp	300mg/100g
Functional Foods	
Liquid eggs (Omega Pro)	900mg/180mL *
Fish Oil Supplements	
Standard	300mg/capsule
Specialty (Omega 600)	600mg/capsule **
* Naturegg (Burnabrae Farms, Lyn, Ont)	
** Clearwater Brand Omega-3 Fish Oil (Ocean Nutrition Canada, Bedford, NS)	

The American Heart Association Guidelines for Healthcare Professionals have included the following recommendations with respect to fish and omega-3 fatty acid supplements:<sup>2</sup>

*'Consumption of one fatty fish meal per day (or alternatively, a fish oil supplement) could result in an omega 3 fatty acid intake (i.e., EPA and DHA) of ~900mg/day, an amount shown to beneficially affect coronary heart disease mortality rates in patients with coronary disease.'*

**Caution:** Certain plant-based omega-3 rich foods and/or supplements containing canola oil, flax/flaxseed oils, walnuts etc. will usually not provide a marked rise in levels of total omega-3 fatty acids or DHA since they contain omega-3 fatty acid as alpha-linolenic acid (ALA), not as EPA/DHA.

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# Group B Streptococcus Screening During Pregnancy

## NEONATAL INFECTION

Group B Streptococcus (GBS) (*Streptococcus agalactiae*) is a significant cause of neonatal morbidity and mortality. Neonatal infection is categorized as early-onset (within 7 days) or late onset (>7 days). Early-onset infection is often associated with maternal risk factors for sepsis such as premature rupture of membranes (PROM), intrapartum fever, and pre-term delivery but also occurs in term infants without any maternal risk factors other than maternal colonization with GBS. Pneumonia, septicemia and meningitis are the most common presentations in early-onset disease. Meningitis or bacteremia without a focus commonly occurs in late-onset neonatal disease.

## EPIDEMIOLOGY

Colonization of the lower genital tract and/or rectum occurs in 15-40% of pregnant women. Cultures taken within 1-5 weeks before delivery are an accurate predictor of colonization status at delivery. GBS is vertically transmitted to the neonate by ascending infection after rupture of membranes or during passage through the birth canal.

## SCREENING AND INTRAPARTUM PROPHYLAXIS FOR GROUP B STREPTOCOCCUS

During the 1990's, several guidelines were published that recommended intrapartum prophylaxis (IPA) for GBS based on either a risk factor approach or GBS culture at 35-37 weeks.<sup>1,2</sup> In an important multicentre, retrospective cohort study,<sup>3</sup> an approach based on culture for GBS at 35-37 weeks gestation was found to prevent more cases of early-onset GBS disease than did a risk-based approach. In addition, compliance with IPA was higher when based on culture results rather than risk based screening.

In 2002, based on the above information, the Centers for Disease Control (CDC) recommended:<sup>4</sup>

- Universal prenatal culture-based screening for vaginal and rectal GBS colonization of all pregnant women at 35-37 weeks gestation.
- IPA for all women with a positive GBS culture.
- If results of GBS culture are not available at the time of delivery, IPA should be guided based on the presence of risk factors.

In contrast to the CDC recommendations, the Canadian Task Force on Preventive Health Care<sup>5</sup> felt that IPA could be given based on a positive culture alone or a positive culture and the presence of risk factors. They felt there was insufficient evidence on the efficacy of IPA based only on the presence of risk factors.

Guidelines from the Society of Obstetricians and Gynecologists of Canada and the Canadian Paediatric Society are in development (personal communication).

## DIAGNOSTIC TESTING

A vaginal-rectal swab for GBS culture and susceptibility testing is preferred for the detection of GBS in pregnant women (see instructions in Table 1). A swab of only the vaginal area is much less sensitive and will miss 10-30% of isolates. A cervical swab is not acceptable. Patient self-collection is comparable to physician sampling provided the patient is provided with clear instructions.<sup>6</sup>

**TABLE 1  
PROCEDURE FOR COLLECTION OF CULTURE  
FOR GROUP B STREPTOCOCCUS**

1. Swab the lower vagina
2. Using the same swab or a different swab, insert swab through the anal sphincter to the rectum
3. Do not use a speculum for collection
4. Place the swab(s) in charcoal or other transport media
5. Store the swab at room temperature
6. Clearly indicate the following: Group B Streptococcus culture, penicillin allergy (if applicable)

**Note:** Isolation of GBS from a urine culture in pregnant patients usually reflects heavy colonization and is an indication for IPA.

## TREATMENT

GBS remains universally susceptible to penicillin and ampicillin. However, in Ontario in 1999, 18% and 8% of isolates were resistant to erythromycin and clindamycin respectively.<sup>7</sup> In the setting of penicillin allergy, susceptibility testing is recommended to guide IPA.

For a urine specimen positive for GBS, if the physician indicates the patient is pregnant and penicillin allergic, susceptibility testing for clindamycin and erythromycin will be performed to guide IPA. However, clindamycin and erythromycin cannot be used to treat urinary tract infection. Amoxicillin remains the treatment of choice for GBS bacteriuria in pregnancy. Clinicians may wish to contact an MDS microbiologist for advice regarding treatment of pregnant patients with penicillin allergy.

GBS screening results should be documented on the antenatal form, as this information must be available to guide IPA at the time of delivery.

## SUMMARY

- Universal screening for GBS colonization is recommended at 35-37 weeks gestation.
- A vaginal-rectal swab is the preferred specimen.
- In pregnant patients at high-risk for anaphylaxis to penicillin, susceptibility testing for clindamycin and erythromycin is indicated on GBS isolates. Clearly indicate that the patient is pregnant and document penicillin allergy (if applicable) on the requisition.

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1. Society of Obstetricians and Gynaecologists of Canada. Statement on the prevention of early onset group B streptococcal infections in newborns. J Soc Obstet Gynaecol Can 1997;19:419-20.
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# Antiphospholipid Antibody Syndrome

Antiphospholipid antibody syndrome (APS) is an immune disease characterized by the presence of antiphospholipid antibodies (APA) and thrombosis or morbidity associated with pregnancy, such as fetal loss.

The most widespread AP antibodies are the Lupus Anticoagulant (LA) and Anticardiolipin Antibodies (ACA) of either the IgG or IgM class. Recent evidence indicates AP antibodies are directed against protein-phospholipid complexes, such as platelet cell surface membranes.

## ANTIPHOSPHOLIPID ANTIBODY PREVALENCE

APA are frequently of no clinical significance. They are found in the general population with a prevalence of 1 to 5%, and more commonly with increased age. The prevalence is much higher in patients with Systemic Lupus Erythematosus (SLE); up to one-third of SLE patients will show ACA and/or LA. In addition, APA may occur in patients with malignancies (lymphoproliferative disease), and in various infections (including syphilis, HIV, Lyme disease, infectious mononucleosis, and tuberculosis).<sup>1-3</sup> These APA are usually transient and not associated with clinical complications. APA may also occur in patients being treated with various drugs (including phenothiazines, procainamide, chlorpromazine, hydralazine, phenytoin and valproic acid).

The estimated yearly incidence of thrombosis in individuals with APA is 1% for those with no history of previous thrombosis, 4% for those with SLE, and 6% for those with high titre IgG AC. LA are more strongly associated with thrombosis than ACA. The presence of LA, and/or medium to high titres of IgG AC helps identify patients at risk for thrombosis.

## DIAGNOSIS OF THE SYNDROME

The diagnostic criteria for APS are the presence of one clinical feature and one of the laboratory criteria as listed in Table 1.<sup>2</sup>

### Clinical Criteria:

The two clinical criteria seen in APS are thrombosis and pregnancy morbidity.

1. Thrombosis consists of one or more clinical episodes of arterial, venous, or small vessel thrombosis in any tissue or organ.
2. There are three categories of pregnancy morbidity:
  - One or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation.
  - One or more premature births of a morphologically normal neonate at or before the 34th week of gestation due to severe pre-eclampsia or eclampsia, or severe placental insufficiency.
  - Three or more unexplained consecutive spontaneous abortions before the 10th week of gestation, following exclusion of both maternal anatomic or hormonal abnormalities and paternal and maternal chromosomal abnormalities.<sup>2</sup>

### Laboratory Criteria:

The two laboratory criteria are the presence and persistence of either ACL or LA.<sup>2</sup>

1. The ACL must be IgG and/or IgM isotype, present in medium or high titre.

2. The screening tests commonly used to detect LA include the activated partial thromboplastin time (aPTT) and the dilute Russell's viper venom time (DRVVT)

The persistence of AC and/or LA is confirmed by two positive tests at least 6 weeks apart.

**Note:** The clinical indication for the tests must be provided on requisition form.

**TABLE 1  
DIAGNOSTIC CRITERIA FOR PRIMARY APS**

#### CLINICAL

Thrombosis or Recurrent fetal loss

#### LABORATORY

1. ACA IgG (>40 GPLu) **or**
2. ACA IgM (>40 GPLu) **and/or**
3. LA test positive – tested by two different methods (e.g. aPTT with mixing studies and DRVVT)

\*At least one clinical and one laboratory finding with demonstration of persistence (RETEST AFTER 6 WEEKS) are required for a definitive diagnosis.

## TREATMENT OF THE SYNDROME

Treatment decisions depend on clinical presentation and fall into four main areas:

- treatment of the acute thrombotic event,
- prevention of further thromboses,
- management of pregnancy, and
- prophylaxis.

Numerous clinical trials have looked at the efficacy and safety of antithrombotic therapy in APS.<sup>1</sup> The underlying disease predisposing the patients to thrombosis must also be treated.

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1. Levine JS, Branch DW, Rauch J. The antiphospholipid syndrome. *N Engl. J. Med.* 2002; 346:752-763.
2. Wilson WA, Gharavi AE, Koike T et al. International consensus on preliminary classification criteria for definite antiphospholipid antibody syndrome. *Arthritis Rheum.* 1999;42: 1309-1311.
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# Ontario Updates

## REFERENCE RANGE CHANGES: 17-HYDROXYPROGESTERONE

Kit reformulation by manufacturer DPC has led to the modification of reference intervals for 17-hydroxyprogesterone.

The revised reference intervals, implemented on August 11, 2003 are as follows:

<b>ADULT MALE</b>	1.8-10.3 nmol/L
<b>ADULT FEMALE</b>	
Follicular phase	0.8-4.2 nmol/L
Luteal phase	1.4-12.8 nmol/L
Postmenopausal	0.6-5.2 nmol/L
Oral Contraceptives	0.5-7.6 nmol/L



## ANTIBODY TO HEPATITIS B SURFACE ANTIGEN

Abbott Diagnostics, the manufacturer of kits used to quantitate antibody to Hepatitis B surface antigen (anti-HBS), has notified laboratories, including MDS, of a problem causing an error in calibration of the assay against the WHO standard. As a result of this bias, patient specimens with values close to the cutoff value for immunity (10.0 IU/L) could be overestimated. To correct this problem, Abbott has introduced re-standardized calibrators that have resulted in a decrease in anti-HBS concentration by approximately 24%. Studies completed within MDS have shown that this change in apparent value may range from 5% - 28%.

For example the result for a patient with an initial value of 12.7 IU/L would now read 9.9 IU/L.

Abbott Diagnostics has indicated that this bias could, potentially, affect calibrator lots from July 2001-July 2003. This problem was beyond our control, however MDS has instituted a search of our database for results within the affected range (10-13 IU/L) and will provide reprints of the reports to clinicians in order to permit the present clinical significance of the information, if any, to be considered.

## CHANGE IN TESTING PROTOCOL FOR METHADONE IN URINE

Effective September 1, 2003, MDS will screen for methadone in urine using the following protocol:

1. Urine specimens will be screened by an immunoassay method specific for the primary metabolite of methadone, EDDP (2-ethylidine-1, 5-dimethyl-3, 3-diphenylpyrrolidine).
2. If the result is positive for EDDP, no further testing is performed and the result is reported as: "Positive for methadone metabolite."
3. If result is negative for EDDP, the specimen is then screened for the presence of methadone by a second immunoassay method. If methadone is present, the test is reported as: "Positive for methadone, negative for methadone metabolite. Interpret result with caution."

The initial measurement of EDDP instead of methadone is based on the rationale that the presence of EDDP in urine is due to in-vivo metabolism of ingested methadone. The new screening approach is useful in monitoring methadone compliance, as well as in allowing the laboratory to aid the clinician in the identification of individuals who add methadone to their urine specimens in an attempt to falsely indicate compliance with the program.

As with all urine drug screens using immunoassay, results should be interpreted as preliminary. We recommend confirmation of all positive results by a more specific technique, high performance liquid chromatography (HPLC). Clinicians requiring confirmatory testing should call MDS Laboratory Services at 416-675-6777, extension 3339 to arrange for this test.

Should you have any questions and/or require further information, please call the MDS Medical or Scientific Staff at 416-675-0637.

continued from *Omega-3*, page 1

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1. Holub B., Clinical Nutrition:4. Omega-3 fatty acids in cardiovascular care. CMAJ 2002; 166(5):608-615.
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4. Lemaitre RN et al. n-3 Polyunsaturated fatty acids, fatal ischemic heart disease, and nonfatal myocardial infarction in older adults: the Cardiovascular Health Study. Am J Clin Nutr 2003; 77: 319-325.