therapeutic apheresis patient. In: McLeod B, Price TH, Weinstein R, editors. *Apheresis: principles and practice*. 2nd ed. Bethesda (MD): American Association of Blood Banks Press; 2003. p. 253-74.
4. Heinisch A, Balle C, Kadow R. Plasmapheresis in severe acute pancreatitis: A new therapeutic option? *Gastroenterology* 1995;108:359.
5. Chen JH, Yeh JH, Lai HW, et al. Therapeutic plasma exchange in patients with hyperlipidemic pancreatitis. *World J Gastroenterol* 2004;10:2272-4.
6. Kadikoylu G, Yavasoglu I, Bolaman Z. Plasma exchange in severe hypertriglyceridemia: a clinical study. *Transfus Apher Sci* 2006;34:253-7.

DOI:10.1503/cmaj.1070056

I wish to provide evidence-based information to correct statements made in the informative and well-written article by George Yuan and colleagues on hypertriglyceridemia[1] with respect to the potential use of omega-3 fatty acids from fish oils to lower triglyceride levels. The authors state that "daily consumption of 4 g of omega-3 fatty acids, along with restricted energy and saturated-fat intakes, can reduce plasma triglyceride levels by as much as 20%. However, omega-3 fatty acids are rarely effective when used as the sole triglyceride-lowering therapy." An earlier review in *CMAJ* outlined evidence for a pronounced effect upon supplementation with docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA).[2] Calculations from the 65 intervention trials reviewed by Harris[3] indicate that plasma triglyceride levels should be reduced by 25%–30% in people with baseline fasting triglyceride levels of 1.70–2.82 mmol/L who take 3 g of supplemental DHA/EPA (combined) per day as their sole triglyceride-lowering therapy. These effects typically occur within 4 weeks in the absence of any significant change in diet. The American Heart Association states that "for individuals with hypertriglyceridemia, 2 to 4 g of DHA/EPA per day, provided as capsules under a physician's care, are recommended."[4]

A reduction in triglyceride levels of 30% or more with 4 g of DHA/EPA per day may be accompanied by a small but significant (5%–10%) increase in low-density lipoprotein cholesterol levels.[3] The indirect determination of low-density lipoprotein cholesterol levels by the Friedewald equation will often yield a small increase whenever triglyceride levels are lowered.

DHA/EPA supplementation should be considered as an additional therapeutic option for hypertriglyceridemia. It is efficacious, safe in most patients and less expensive than most other therapies for triglyceride management, and patient compliance is usually good.[5] A recent review concluded that combination therapy with statins and DHA/EPA supplementation has been "consistently shown to be an effective, safe, and well-tolerated treatment for combined dyslipidemia."[6]

Bruce J. Holub PhD
Professor Emeritus
Department of Human Health and Nutritional Sciences
University of Guelph
Guelph, Ont.

Competing interests: Bruce Holub is Director of Scientific Affairs for the DHA/EPA Omega-3 Institute (www.dhaomega3.org). Croda Inc., Ocean Nutrition Canada Ltd. and EPAX AS, manufacturers of omega-3 fish oil concentrates containing DHA/EPA, provide support to the Institute. In the past year, Dr. Holub has received a speaker fee from EPAX and from Mead Johnson Nutritionals.

REFERENCES

1. Yuan G, Al-Shali KZ, Hegele RA. Hypertriglyceridemia: its etiology, effects and treatment. *CMAJ* 2007;176:1113-20.
2. Holub BJ. Clinical nutrition: 4. Omega-3 fatty acids in cardiovascular care. *CMAJ* 2002;166:608-15.
3. Harris WS. n-3 Fatty acids and serum lipoproteins: human studies. *Am J Clin Nutr* 1997;65(Suppl):1645S-1654S.
4. Lichtenstein AH, Appel LJ, Brands, M, et al. Diet and lifestyle recommendations revision 2006: a scientific statement from the American Heart Association Nutrition Committee. *Circulation* 2006;114(1):82-96.
5. Pejic RN, Lee DT. Hypertriglyceridemia. *J Am Board Fam Med* 2006;19(3):310-6.
6. Nambi V, Ballantyne CM. Combination therapy with statins and omega-3 fatty acids. *Am J Cardiol* 2006;98(4A):34i-38i.

DOI:10.1503/cmaj.1070064

[Two of the authors respond:]

We appreciate the interest that the correspondents have shown in our review of hypertriglyceridemia.[1] Our comment regarding the relative ineffectiveness of fish oil as monotherapy was provided in the context of the treatment of severe hypertriglyceridemia. We agree with Bruce Holub's comments regarding the efficacy of DHA and EPA for milder presentations of hypertriglyceridemia, and Table 2 of our article reflects this position. We also accept the potential efficacy of the combination of DHA and EPA with statin drugs in patients with combined hyperlipidemia. However, this combination awaits evaluation in larger prospective controlled studies.

Ifran Yavasoglu and colleagues and Georg Röggla and colleagues report dramatic improvements in severe hypertriglyceridemia associated with the use of plasma exchange and insulin and heparin administration, respectively. We also observed apparently dramatic biochemical improvement associated with heparin infusion.[2] However, our clinical experience with patients who have serum triglyceride concentrations greater than 20 mmol/L, often accompanied by acute pancreatitis, is that admission to hospital with cessation of oral intake and appropriate intravenous fluid replacement (with or without insulin therapy depending on the presence of hyperglycemia) is typically followed by a rapid reduction in plasma triglyceride levels irrespective of other treatment modalities.

When oral food and fluids are withheld, a clinical rule of thumb is that triglyceride levels decay exponentially with a half-life of approximately 48 hours. This is comparable to the reductions observed by Yavasoglu and colleagues for plasma exchange and by Röggla and colleagues for a combined insulin and heparin regimen. Controlled, randomized studies, although logistically challenging, would be required to define the risk versus benefit to patients with severe hypertriglyceridemia of either plasma exchange or routine infusions of insulin or heparin. Until then, we stand by our position that these modalities should be used sparingly, if at all, in this situation.

George Yuan BSc
Schulich School of Medicine and Dentistry
Robert A. Hegele MD
Robarts Research Institute
University of Western Ontario
London, Ont.

Competing interests: None declared.

REFERENCES

1. Yuan G, Al-Shali KZ, Hegele RA. Hypertriglyc-