large thrombus burden. Indeed, a recent study comparing clinical and procedural characteristics among hospitals, mostly regarding elective percutaneous coronary intervention, invariably reported a contrast volume of more than 200 ml.<sup>5</sup>

Finally, the difference in the primary end point and the other clinical end points between the two *N*-acetylcysteine groups was significant when analyzed by the Mantel–Haenszel chi-square test for trend, suggesting a dose-dependent protective effect of *N*-acetylcysteine.

Giancarlo Marenzi, M.D. Gianfranco Lauri, M.D. Antonio L. Bartorelli, M.D. Centro Cardiologico Monzino 20138 Milan, Italy giancarlo.marenzi@ccfm.it

1. Carrabba N, Santoro GM, Balzi D, et al. In-hospital manage-

ment and outcome in women with acute myocardial infarction (data from the AMI-Florence Registry). Am J Cardiol 2004;94: 1118-23.

**2.** Zahn R, Vogt A, Zeymer U, et al. In-hospital time to treatment of patients with acute ST elevation myocardial infarction treated with primary angioplasty: determinants and outcome: results from the registry of percutaneous coronary interventions in acute myocardial infarction of the Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausarzte. Heart 2005;91:1041-6.

**3.** Yamaguchi J, Kasanuki H, Ishii Y, et al. Prognostic significance of serum creatinine concentration for in-hospital mortality in patients with acute myocardial infarction who underwent successful primary percutaneous coronary intervention (from the Heart Institute of Japan Acute Myocardial Infarction [HIJAMI] Registry). Am J Cardiol 2004;93:1526-8.

4. McCullough PA, Soman SS. Epidemiology and predictors of contrast-induced nephropathy. In: Bartorelli AL, Marenzi G, eds. Contrast-induced nephropathy: in interventional cardiovascular medicine. London: Taylor & Francis, 2005:19-33.

**5.** Moscucci M, Share D, Smith D, et al. Relationship between operator volume and adverse outcome in contemporary percutaneous coronary intervention practice: an analysis of a quality-controlled multicenter percutaneous coronary intervention clinical database. J Am Coll Cardiol 2005;46:625-32.

## Iodine Nutrition — More Is Better

TO THE EDITOR: The editorial by Utiger (June 29 issue)1 summarizes the effects of iodine deficiency. However, his recommendation of an iodine intake of 300 to 400  $\mu$ g per day far exceeds the following recommendations of the Institute of Medicine: 150  $\mu$ g per day for nonpregnant adults, 220  $\mu$ g per day for pregnant women, and 290  $\mu$ g per day during lactation.<sup>2</sup> Teng et al.<sup>3</sup> found that an iodine intake of approximately 320 to 840  $\mu g$ per day resulted in an increased incidence of subclinical hypothyroidism and thyroid autoimmunity. These risks may be clinically important children of women with subclinical gestational hypothyroidism may have neurocognitive delays.<sup>4</sup> Utiger suggests that iodine intake in the United States is marginal on the basis of the prevalence of spot urinary iodine values under 50  $\mu$ g per liter among pregnant women.<sup>5</sup> However, iodine deficiency may not be diagnosed from analysis of spot urine samples in individuals because of day-to-day variability. Median spot urinary iodine values accurately reflect the iodine nutrition of populations, and the median value of 168  $\mu$ g per liter for the United States<sup>5</sup> is consistent with iodine sufficiency according to World Health Organization (WHO) criteria. We believe

that the evidence supports the current guidelines for dietary iodine intake and that overall iodine intake in the United States remains sufficient.

Elizabeth N. Pearce, M.D. Boston University Medical Center Boston, MA 02118 elizabeth.pearce@bmc.org Joseph G. Hollowell, Jr., M.D., M.P.H. University of Kansas Medical Center Lawrence, KS 66120

1. Utiger RD. Iodine nutrition — more is better. N Engl J Med 2006;354:2819-21.

**2.** Food and Nutrition Board Institute of Medicine. Dietary reference intakes. Washington, DC: National Academy Press, 2001.

**3.** Teng W, Shan Z, Teng X, et al. Effect of iodine intake on thyroid diseases in China. N Engl J Med 2006;354:2783-93.

**4.** Haddow JE, Palomaki GE, Allan WC, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med 1999;341:549-55.

**5.** Caldwell KL, Jones R, Hollowell JG. Urinary iodine concentration: United States National Health and Nutrition Examination Survey 2001-2002. Thyroid 2005;15:692-9.

**TO THE EDITOR:** We fully agree with the title of Utiger's editorial, "Iodine Nutrition — More Is Better," but wish to comment on how much more is better during pregnancy and lactation.

In January 2005, the WHO held a technical

The New England Journal of Medicine

Downloaded from nejm.org at CSIC on September 5, 2013. For personal use only. No other uses without permission.

Copyright © 2006 Massachusetts Medical Society. All rights reserved.

consultation on this point, and one of us was an invited speaker. The recommendation that emerged was for pregnant and lactating women to have 250 instead of 200  $\mu$ g of iodine daily,<sup>1</sup> almost double the intake for the adult population. This results in urinary concentrations of 150 to 250  $\mu$ g of iodine per liter. Even in areas with marginal iodine intake, the United States and Spain included (Fig. 1 of the editorial), it is highly unlikely that pregnant and lactating women receive enough iodine<sup>2</sup> for normal fetal neurodevelopment,<sup>3</sup> unless daily supplements (i.e., 200  $\mu$ g of iodine) are prescribed from the onset of pregnancy (or before). Such supplements taken during pregnancy and lactation would overcome changes of iodine intake through food and iodinated salt that frequently occur after conception. Supplementation is being implemented in Spain, where Yoduk tablets containing 200  $\mu$ g of iodine (262  $\mu$ g of potassium iodide) are made available to pregnant and lactating women through the National Health System.

Gabriella Morreale de Escobar, Ph.D. Francisco Escobar del Rey, M.D., Ph.D.

Instituto de Investigaciones Biomédicas Alberto Sols 28029 Madrid, Spain gmorreale@iib.uam.es

1. DeBenoist B, Delange F. Report of a WHO technical consultation on prevention and control of iodine deficiency in pregnancy, lactation and in children, less than 2 years of age. Public Health Nutr (in press).

**2.** Morreale de Escobar G, Obregón MJ, Escobar del Rey F. Role of thyroid hormone during early brain development. Eur J Endocrinol 2004;151:Suppl 3:U25-U37.

**3.** *Idem.* Maternal thyroid hormones early in pregnancy and fetal brain development. Best Pract Res Clin Endocrinol Metab 2004;18:225-48.

**THE EDITORIALIST REPLIES:** My recommendation that daily iodine intake should be 300 to 400  $\mu$ g does exceed the recommendations of the Institute of Medicine by a factor of two for men and non-pregnant women, and less for pregnant and lactating women, but it does not far exceed them, as stated by Drs. Pearce and Hollowell. My recommendation was based on my concern about the increase by a factor of seven (from 1 to 7 percent) in the frequency of moderate iodine deficiency among pregnant women and also the increase by a factor of 5 to 12 percent) in the frequency from 3 to 12 percent) in the frequency of moderate increase by a factor of seven (from 3 to 12 percent) in the frequency frequency in the frequency of moderate increase by a factor of four (from 3 to 12 percent) in the frequency frequency in the frequency in the frequency frequency in the frequency in the frequency in the frequency frequency in the freq

quency of moderate iodine deficiency in the total population, coincident with the decline of more than 50% in urinary iodine excretion in the United States from 1971–1974 to 1988–1994 (and from 1971–1974 to 2001–2002).<sup>1</sup> Raising the iodine intake to 300 to 400  $\mu$ g daily should reduce the frequency of low values to the 1971–1974 levels.

Drs. Morreale de Escobar and Escobar del Rey endorse the need for increased iodine intake in pregnant women, and point out another way to achieve this. All prenatal vitamin preparations should contain iodine, and all pregnant women should take them. My preference, however, is to increase iodine intake for everyone.

As noted by Drs. Pearce and Hollowell, day-today urinary iodine excretion varies within subjects.<sup>2</sup> However, low values cannot be dismissed as an exceptional finding; they are biologically important. For example, pregnant women with urinary iodine values of less than 50  $\mu$ g per liter had larger thyroid glands and higher serum thyrotropin and thyroglobulin concentrations, indicative of compensatory thyroid stimulation, than did pregnant women who were given a supplement of 100  $\mu$ g of iodine daily.<sup>3</sup> Similarly, at birth, their infants had larger thyroid glands and higher serum thyroglobulin concentrations than did the infants of mothers who received the supplement. Although higher iodine intakes may be associated with very small increases in the prevalence and incidence of subclinical hypothyroidism and autoimmune thyroiditis,4 it is more important to ensure that everyone, especially pregnant women, has an adequate iodine intake.

Robert D. Utiger, M.D.

Brigham and Women's Hospital Boston, MA 02115

1. Hollowell JG, Staehling NW, Hannon WH, et al. Iodine nutrition in the United States: trends and public health implications: iodine excretion data from National Health and Nutrition Examination Surveys I and III (1971-74 and 1988-1994). J Clin Endocrinol Metab 1998;83:3401-8.

2. Busnardo B, Nacamulli D, Zambonin L, Mian C, Piccolo M, Cirelli ME. Restricted intraindividual urinary iodine concentration variability in nonfasting subjects. Eur J Clin Nutr 2006;60: 421-5.

**3.** Glinoer D, De Nayer P, Delange F, et al. A randomized trial for the treatment of mild iodine deficiency during pregnancy: maternal and neonatal effects. J Clin Endocrinol Metab 1995;80: 258-69.

**4.** Teng W, Shan Z, Teng X, et al. Effect of iodine intake on thyroid diseases in China. N Engl J Med 2006;354:2783-93.