

sartan group than in the captopril group (1.4 percent vs. 0.8 percent; excess, 6 per 1000; $P < 0.05$). However, discontinuation because of any adverse event was more frequent in the captopril group (7.7 percent, vs. 5.8 percent in the valsartan group; excess, 19 per 1000; $P < 0.05$). We are conducting a more detailed analysis to attempt to identify patient characteristics associated with a heightened risk of specific drug-related adverse events. The different side-effect profiles of these two effective alternative approaches should assist clinicians in individualizing therapy to extend the appropriate

use of these lifesaving interventions to more survivors of myocardial infarction.

Marc A. Pfeffer, M.D., Ph.D.

Brigham and Women's Hospital
Boston, MA 02115
mpfeffer@rics.bwh.harvard.edu

John J.V. McMurray, M.D.

Western Infirmary
Glasgow G11 6NT, Scotland

Robert M. Califf, M.D.

Duke University Medical Center
Durham, NC 27710

The Toxicology of Mercury

TO THE EDITOR: As a public health official who has been raising the consciousness of my community with regard to the potential hazards of eating mercury-containing fish, I am disturbed by the review article on mercury by Clarkson and colleagues (Oct. 30 issue).¹ The Environmental Protection Agency, the Food and Drug Administration, and the health departments of most states have not published advisories or reference doses on mercury in fish, for nebulous reasons. Over the past 30 years, the level of mercury that we know is associated with a harmful effect has declined significantly, as has the regulatory standard for what is considered a "safe" level of exposure. Certainly there are safe and healthy alternatives to the use of mercury-containing dental amalgams, as there are to the consumption of fish containing high mercury levels. The authors' conclusions that the health effects of a low level of mercury exposure are "open to wide interpretation" and that "attempts to reduce such exposure may pose greater health risks than those hypothesized to occur from mercury" sound like conclusions that might be drawn by the electric power or tuna industry.

Lawrence S. Block, M.D.

Swampscott Board of Health
Swampscott, MA 01907
lblock@partners.org

1. Clarkson TW, Magos L, Myers GJ. The toxicology of mercury—current exposures and clinical manifestations. *N Engl J Med* 2003; 349:1731-7.

TO THE EDITOR: Clarkson et al. find no hazard to adults or children in the United States from routine dietary, dental, or pharmaceutical sources of mer-

cury. The authors discount the findings of neuro-behavioral and cardiovascular abnormalities in the offspring of women with blood mercury levels at the upper limit for American women of childbearing age.^{1,2} However, each year, an estimated 84,300 pregnant women eat more than 100 g of fish per day.³ Pregnant and lactating women should not have to limit their intake of economical, healthy protein. Environmental policymakers must strive to reduce environmental mercury levels so that existing fish-consumption advisories will not be needed. The Massachusetts Medical Society has advocated for reductions in mercury emissions from power plants, a major source of environmental mercury in fish.⁴ We support strict efforts to control mercury and other hazardous emissions from coal- and oil-fired power plants. The adoption of less strict emission standards could result in higher mercury levels in the food supply of Americans.

Bill Patterson, M.D., M.P.H.

Occupational Health and Rehabilitation
Hingham, MA 02043

James Ryan, M.D., M.P.H.

Boston Medical Center
Boston, MA 02118

Jefferson H. Dickey, M.D.

51 Sanderson St.
Greenfield, MA 01301

1. Murata K, Budtz-Jorgensen E, Grandjean P. Benchmark dose calculations for methylmercury-associated delays on evoked potential latencies in two cohorts of children. *Risk Anal* 2002;22:465-74.
2. Sorenson N, Murata K, Budtz-Jorgensen E, Weihe P, Grandjean P. Prenatal methylmercury exposure as a cardiovascular risk factor at seven years of age. *Epidemiology* 1999;10:370-5.
3. Mercury study report to Congress. Vol. 6. An ecological assessment for anthropogenic mercury emissions in the United States.

Washington, D.C.: Environmental Protection Agency, December 1997. (EPA-452/R-97-008.)

4. Mercury. In: Massachusetts Medical Society policy compendium, 2003 edition. Waltham, Mass.: Massachusetts Medical Society, 2003. (Accessed February 6, 2004, at <http://www.massmed.org/about/policies/environment.asp>.)

TO THE EDITOR: Magical-religious and ethnomedical use of elemental mercury is a major source of exposure in some Caribbean and Hispanic communities. Clarkson et al. refer to these exposures only in passing, although they are widespread and clinically significant. Between 25,000 and 155,000 mercury capsules (mean weight per capsule, 9 g) were sold for ritualistic use in the Bronx, New York, in 1995, with some 30 percent of informants recommending that mercury be sprinkled on floors.¹ Another study found that 5 of 100 Bronx children had elevated urinary mercury levels.² Mercury vapor levels in Hispanic housing were elevated in comparison with those in control housing.³ Ritualistic use of mercury was the median source of mercury influx to the New York–New Jersey harbor.⁴ Clarkson et al. state that “ingested liquid mercury [is] essentially unabsorbed,” whereas 0.01 percent is absorbed⁵ (or 1 mg retained) of a 10-g dose ethnomedically administered to an infant for stomach upset. The National Center for Environmental Health of the Centers for Disease Control and Prevention will shortly measure urinary mercury levels in 250 Hispanic children in the Bronx. Clinicians serving Hispanic and Caribbean communities should be alert to signs and symptoms of these exposures.

Arnold P. Wendroff, Ph.D.

Mercury Poisoning Project
Brooklyn, NY 11215
mercurywendroff@mindspring.com

1. Zayas LH, Ozuah PO. Mercury use in espiritismo: a survey of boricans. *Am J Public Health* 1996;86:111-2.
2. Ozuah PO, Lesser MS, Woods JS, Choi H, Markowitz M. Mercury exposure in an urban pediatric population. *Ambul Pediatr* 2003;3:24-6.
3. Stern AH, Gochfeld M, Riley D, Newby A, Leal T, Garetano G. Cultural uses of mercury in New Jersey. Research project summary. Environmental assessment and risk analysis element. Trenton: Division of Science Research and Technology, New Jersey Department of Environmental Protection, May 2003.
4. de Cerreno ALC, Panero M, Boehme S. Pollution prevention and management strategies for mercury in the New York/New Jersey harbor. New York: New York Academy of Sciences, May 2002.
5. Clarkson T, ed. Mercury toxicity. Case studies in environmental medicine. No. 17. Atlanta: Agency for Toxic Substances and Disease Registry, March 1992.

TO THE EDITOR: Having recently worked in public health research in Mwanza, Tanzania, which is within the goldfields of the Lake Victoria basin, I

expected that the review by Clarkson et al. would contain information on the health risks associated with the widespread use of mercury to extract gold from ore. This method is used by most small-scale gold miners throughout the world and usually involves both direct handling of mercury and inhalation of mercury vapor as the mercury–ore mixture is heated over an open flame during the extraction process. A recent review concluded that “miners who used elemental mercury to amalgamate and extract gold were heavily contaminated with mercury.”¹

Hundreds of thousands of people are engaged in small-scale gold mining, mainly in relatively remote areas of developing countries, with little if any knowledge of the health risks they face from mercury. The connection between the use of mercury and its insidious toxic effects is difficult to perceive and is usually missed by health workers and sufferers alike.

David A. Ross, B.M., B.Ch., Ph.D.

London School of Hygiene and Tropical Medicine
London WC1E 7HT, United Kingdom
david.ross@lshtm.ac.uk

1. Eisler R. Health risks of gold miners: a synoptic review. *Environ Geochem Health* 2003;25:325-45.

TO THE EDITOR: Clarkson et al. imply that there might be consequences for the health of dental patients if the use of mercury-containing dental amalgam were to be curtailed. Advances in dental materials over the past 20 years have rendered amalgam potentially obsolete, although some dentists continue to use it. Composite dental filling materials of micron-sized glass particles bound in resin have been proved durable, economical, easy to use, and popular with patients because of their natural appearance. They present far less potential for toxicity than amalgam, which, as the authors acknowledge, releases mercury vapor on a continuous basis. The majority of dental fillings in the United States in the past few years are reported to have been performed with the use of composites. The dental profession is now in a position to leave the age of mercurial remedies behind.

Stephan M. Koral, D.M.D.

2006 Broadway
Boulder, CO 80302

THE AUTHORS REPLY: Our article focused on the three species of mercury to which billions of people are exposed: methyl mercury in fish; mercury vapor from dental amalgam; and ethyl mercury (in

the form of thimerosal), present as a preservative in many commonly used vaccines and some immune globulins. Although mercury in all these forms is toxic, the question is whether sufficient amounts can be absorbed from these sources to produce toxic effects. Moreover, each source of mercury is associated with beneficial use. Fish consumption lowers the risk of coronary heart disease¹ and perhaps even the risk of Alzheimer's disease.² Dental amalgam remains a safe and effective tooth filling. Thimerosal in vaccines makes possible the use of multiple-dose vials, which remain essential in developing countries. Our point was that further attempts to reduce exposure to these forms of mercury present a dilemma, because they require that the health risks from mercury itself be balanced against the loss of the beneficial outcomes.

Two letter writers decry what they see as our underplaying of health risks from methyl mercury in fish. Our article questioned some of the evidence for health risks from the three sources of exposure to mercury. This uncertainty in risk estimates further emphasizes the dilemma.

Another writer claims that dental amalgam is associated with higher health risks than alternative fillings. The issue we addressed was that of replacing amalgam fillings already placed in teeth. The process of removal elevates mercury levels to peak heights that are about double the preremoval levels. In any case, alternatives to dental-amalgam fill-

ings are not a panacea, as is shown by reports of leakage and wear.^{3,4}

Two letters alert us to other routes of exposure to mercury vapor — namely, the use of liquid mercury to extract gold from river sediments and the ethno-religious uses of quicksilver in homes. We agree that these two uses can lead to high exposures and overt poisoning, but they do not present a dilemma to the health profession. Such uses of mercury clearly should be discontinued.

Tom Clarkson, Ph.D.

University of Rochester
Rochester, NY 14642
twc30@aol.com

Laszlo Magos, M.D.

Medical Research Council
Wallington SM6 0TE, United Kingdom

Gary Myers, M.D.

University of Rochester
Rochester, NY 14642

1. Hu FB, Bronner L, Willett WC, et al. Fish and omega-3 fatty acid intake and risk of coronary heart disease in women. *JAMA* 2002; 287:1815-21.

2. Morris MC, Evans DA, Bienias JL, et al. Consumption of fish and n-3 fatty acids and risk of incident Alzheimer disease. *Arch Neurol* 2003;60:940-6.

3. Jain P, Pershing A. Depth of cure and microleakage with high-intensity and ramped resin-based composite curing lights. *J Am Dent Assoc* 2003;134:1215-23.

4. Kubo S, Yokota H, Yokota H, Hayashi Y. Effect of low-viscosity resin-based composite on microleakage of cervical restorations. *Am J Dent* 2003;16:244-8.

Gene Silencing

TO THE EDITOR: Herman and Baylin (Nov. 20 issue)¹ provide an excellent review of gene silencing in cancer in association with promoter hypermethylation. However, some readers who are new to the field will be confused by the introductory section of their article — in particular, the authors' explanation of the term "epigenetic," which suggests that this term describes "a heritable change in the pattern of gene expression." In fact, in this context, promoter hypermethylation is a somatic event, and although it may be passed on to daughter somatic cells, it is not heritable in the germ line. Although it is later stated that "epigenetic change is not a mechanism of the first hit" in familial cancer, the introductory summary may be misleading.

Judy Kirk, M.B., B.S.

Westmead Hospital
2145 Sydney, Australia
judy_kirk@wmi.usyd.edu.au

1. Herman JG, Baylin SB. Gene silencing in cancer in association with promoter hypermethylation. *N Engl J Med* 2003;349:2042-54.

THE AUTHORS REPLY: We thank Dr. Kirk for her thoughtful comments regarding the definition of the term "epigenetic" in our review. She is certainly correct in stating that the heritable patterns defined by this term generally refer to gene-expression changes not based on changes in the DNA base sequence and that they are passed on to daughter cells in a somatic-cell, rather than a germ-cell, context. Thus, DNA-methylation patterns are heritable through cell division but are usually not hereditary in the sense of being passed on through meiosis. It should be noted, however, that there are DNA-methylation patterns, and attendant gene silencing, that are perpetuated in somatic cells from