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Breaking America's Dependence on Imported Molybdenum

Andrew J. Einstein, MD, PhD, FACC

Approximately 9 million nuclear cardiology studies performed each year in the U.S. use technetium-99m, which is produced from the decay of molybdenum-99. The fragility of the worldwide technetium-99m supply chain has been underscored by current shortages caused by an unplanned shutdown of Europe's largest reactor. The majority of the U.S. supply derives from a reactor in Canada that is nearing the end of its lifespan and whose planned replacements have been cancelled recently. In this article, the clinical importance of technetium-99m and our tenuous dependence on the foreign supply of molybdenum are addressed, along with potential measures that may be taken to ensure that America's supply chain remains unbroken.

With gasoline prices reaching record highs last year, Americans have become keenly aware of our reliance on foreign oil. In hindsight, earlier attention to developing alternative energy sources may have averted the consequences of this dependence.

Lost amid the news about oil prices is another type of energy crisis in the making. The recent announcement by an obscure state-controlled Canadian company that it had discontinued plans to develop 2 nuclear reactors has garnered virtually no attention, but it should be of great concern to all, and to cardiologists in particular. This announcement sets the stage for an impending crisis in our nation's radioisotope supply, leading to difficult triage decisions, delayed procedures, and worse outcomes in some patients for whom clinically indicated imaging will be denied, deferred, or performed suboptimally. Thankfully, unlike for oil, this is a situation in which we still have time to act before paying the serious consequences of foreign dependence.

Roughly 40 million nuclear medicine procedures are performed worldwide each year, with one-half of these in the U.S. The most commonly performed nuclear medicine test, accounting for one-half of all nuclear medicine procedures, is the myocardial perfusion imaging study. In the U.S., approximately 9 million such nuclear stress tests are performed each year (1).

Although there are many radioisotopes used in nuclear medicine, the field's workhorse is technetium-99m (Tc-99m), which is incorporated into over 30 different radiopharmaceuticals. Approximately 4 of 5 patients undergoing nuclear medicine studies receive a Tc-99m–based radiopharmaceutical (2), including 97% of patients undergoing nuclear stress testing (1). For myocardial perfusion imaging, Tc-99m–labeled perfusion tracers offer several advantages over their common alternative, thallium-201 (Tl-201), which is cyclotron produced and has witnessed a steady decline in use during recent years (1). Attenuation of photons

From the Department of Medicine, Cardiology Division, and Department of Radiology, Columbia University College of Physicians and Surgeons, New York, New York. Dr. Einstein is supported in part by an NIH K12 institutional career development award (5 KL2 RR024157-03). Dr. Einstein reports receiving an American Society of Nuclear Cardiology/Nuclear Cardiology Foundation research grant that was sponsored by Covidien (Covidien's support was only disclosed to Dr. Einstein after receiving the grant), consulting fees from GE Healthcare (unrelated to GE's SPECT, PET or radiopharmaceutical units), and travel expenses covered by GE Healthcare, INVIA, Philips Medical Systems, and Toshiba America Medical Systems.

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Table 1. Major Worldwide Reactors Producing Mo-99 and Their Distributors

Reactor	Location	Owner*	Operation (Days/Year)	Mo-99 Distributor	Percent of Worldwide Mo-99 Supply
National Research Universal (NRU)	Chalk River, Canada	Canada	315	MDS-Nordion	40
High Flux Reactor (HFR)	Petten, the Netherlands	European Union	290	Covidien	20
				IRE	10
South African Fundamental Atomic Reactor Installation-1 (SAFARI-1)	Pelindaba, South Africa	South Africa	315	NTP	10
Belgian Reactor-2 (BR2)	Mol, Belgium	Belgium	115	Covidien	5
				IRE	4
OSIRIS	Saclay, France	France	220	IRE	3

*Through government's solely owned entity or public utility. The data are representative for 2004. Capacity Mo-99 production is the maximum that the reactor could produce by irradiating during a full week the maximum load of targets. Adapted from Bonet et al (2).
IRE = Institut National des Radioéléments, Belgium; NTP = Nuclear Technology Products, owned by South Africa.

as a function of soft-tissue depth is a potential limitation of Tl-201 in patients with large body habitus. In addition, because of the long physical half-life of Tl-201, the amount of thallium administered to a patient is confined by its radiation burden (3). Although there are alternative myocardial perfusion tracers, such as rubidium-82 and N-13 ammonia, imaging these perfusion tracers requires positron emission tomography, which is not as readily available as the single-photon emission tomography cameras used for imaging Tc-99m and Tl-201.

Tc-99m is produced from the decay of molybdenum-99 (Mo-99). Because the half-life of Mo-99 is only 66 h, it cannot be stockpiled and, therefore, the medical benefits of Tc-99m are dependent on a reliable and continuous supply chain of Mo-99. More than 90% of the world's supply of Mo-99 derives from the irradiation of uranium targets at 5 nuclear reactors in Canada, Belgium, the Netherlands, France, and South Africa (Table 1) (2). There has not been a U.S. source capable of producing significant amounts of Mo-99 in 2 decades (4,5).

The majority of the Mo-99 used in this country is imported from Canada, where it is produced at a reactor in Chalk River, Ontario, before processing. This National Research Universal (NRU) reactor is now more than 50 years old. It was slated to be replaced with 2 new reactors, referred to as MAPLE (Multipurpose Applied Physics Lattice Experiment) reactors. These completed construction in 2000 but were never commissioned for use. After 8 years of design flaws, budget overruns, and safety concerns, Atomic Energy of Canada Limited cancelled the program in May 2008, deeming the new reactors not feasible to operate, and the Canadian government subsequently announced that the decision is final.

This leaves America's Mo-99 supply dependent on the old NRU reactor, which has been subject to multiple shutdowns. A planned 4-day maintenance shutdown in November 2007 was extended to 4 weeks as the result of safety concerns, leading to molybdenum shortages and the intervention of Prime Minister Stephen Harper to restart production before completion of a mandated safety upgrade. A current industry estimate is that the NRU, which was originally scheduled to close in 2005, could last until 2014 (6). This continuation would require an extension of the current operating license, which expires in 2011, and further safety concerns could arise at reinspection.

After the NRU ceases operations, the 4 other high-capacity reactors could not ramp up production to meet worldwide molybdenum demand for a stretch of more than a few weeks. Moreover, each is at least 40 years old, and transport of molybdenum from these facilities across the Atlantic is associated with sizable radioactive decay, requiring more isotope at greater cost. The fragility of the worldwide molybdenum supply has been further underscored by the temporary closure in August 2008 of each of the 5 major reactors producing Mo-99 (7). Four reactors, including the NRU, were down for scheduled maintenance, and the reactor in the Netherlands that produces the majority of Europe's molybdenum and is the second largest source for the U.S. was down as the result of a leak into its cooling system caused by corrosion of its pipe work (8). This situation, which at the time of this writing is expected to last until February 2009, has led to a decrease in the supply of Tc-99m generators available in the U.S. In Europe, which is more dependent on the Dutch reactor, more pronounced shortages and rationing have occurred, a harbinger for what we can expect here post-NRU unless a good solution is in place.

The long-term solution to the U.S. molybdenum needs is a domestic source. This solution has been recognized by professional societies for more than a decade and has been recommended by multiple advisory committees, most recently in a National Academies report published a year ago (9) and a recent letter from the Nuclear Energy Advisory Committee offering recommendations to the Department of Energy (10). We are now in the end-game in terms of the current mo-

lybdenum supply chain, and how we play it will determine whether Americans have a continuous supply of Tc-99m or a crisis in which patients are unable to obtain essential medical tests.

An interrelated issue is that each of the 5 major reactors producing Mo-99 uses highly enriched uranium targets, which contain at minimum 36% and, in most cases, 93% uranium-235. Highly enriched uranium is considered by many experts to be a global nonproliferation concern (11). The Energy Policy Act of 2005 mandated a National Academy of Sciences study, due in December 2008, that is investigating the possibilities for—and cost-effectiveness of—providing for the nation's medical isotope needs from sources that do not use highly enriched uranium (12).

Fortunately, there are potential solutions to America's molybdenum needs. One would be for governmental support of domestic low-enrichment uranium-based molybdenum production. A research reactor already in place could be adapted to provide at least one-half of U.S. Mo-99 demand, although this would require capital to build a processing facility, which would cost an estimated $40 million. Most likely this would necessitate federal funding, probably through the Department of Energy. Such funding, which is advocated in the Nuclear Energy Advisory Committee's letter to the Secretary of Energy (10), would require a change in the current language in the Senate's proposed 2009 Energy and Water Development and Related Agencies Appropriations Act, which provides for a feasibility study (13) but not for development of a processing facility.

Another strong possibility for a domestic molybdenum source, although likely on a longer timetable, is an effort in the private sector to develop a novel type of reactor technology, called an aqueous homogenous reactor, in which uranium dissolved in water and acid serves as both the reactor's target and fuel. An aqueous homogenous reactor would generate significantly less radioactive waste than do current processes. Both of these potential solutions to our molybdenum needs would use low-enriched uranium targets for molybdenum production.

With the cancellation of the MAPLE reactor project, it is clear that the present U.S. Mo-99 supply chain is not sustainable for the long term, and thus it is imperative that we explore potential domestic sources. Our continued ability to provide the best health care to our patients lies in the balance.

Reprint requests and correspondence to: Dr. Andrew J. Einstein, Columbia University Medical Center, 622 West 168th Street, PH 10-203A, New York, New York 10032. *E-mail: andrew.einstein@columbia.edu.*

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