Museu Nacional, Universidade Federal do Rio de Janeiro, Quinta da Boa Vista, São Cristóvão, Rio de Janeiro, RJ, 20940-040, Brazil. [2]Museu de Ciências da Terra, Departamento Nacional de Produção Mineral, avenida Pasteur 404, Rio de Janeiro, RJ, 22290-240, Brazil.

Reference
1. D. R. Carrier, S. M. Deban, J. Otterstrom, *J. Exp. Biol.* **205**, 1755 (2002).

Humility in Observational Studies

THE WOMEN'S HEALTH INITIATIVE HORMONE replacement therapy (HRT) study has shaken medical practice and left many women puzzling, as reflected in Martin Enserink's article "The vanishing promises of hormone replacement" (News Focus, 19 July, p. 325). Although many previous observational studies found substantial cardio-protection with HRT (*1*), two large, well-conducted clinical trials found no such "protection" (*2*, *3*). Why were these earlier studies wrong? In all likelihood, although the observational studies "controlled" for a plethora of variables, they all suffered the same "selection bias"—women using HRT were healthier in other ways those studies didn't or couldn't address well.

Beyond HRT itself, however, the studies are a wake-up call for a range of disciplines including sociology, demography, epidemiology, and econometrics that often rely on such observational methods and attempt to "control" for variables statistically. For example, education is associated with positive social attributes including economic status, voter participation, lower cardiovascular disease, lower infant mortality, and lower fertility. So education is advocated for those benefits. But investigators seldom pursue how people who achieve higher education might be different (e.g., in motivation, intelligence, work ethic, aspirations, social connections, and so forth) and thus confound the effect of education. Rather this entire Gordion knot of explanatory factors is often lumped together as years of schooling.

No single study design is a panacea. We must continue to use such observational methodologies. But we must implement them more carefully and interpret them more humbly.

JAMES D. SHELTON*
Senior Medical Scientist, Bureau for Global Health, Office of Population and Reproductive Health, Agency for International Development, Ronald Reagan Building, Washington, DC 20523–1000, USA. E-mail: JShelton@USAID.GOV
*The views expressed are not necessarily those of USAID.

References
1. D. Grady *et al.*, *Ann. Intern. Med.* **117**, 1016 (1992).
2. Writing Group for the Women's Health Initiative Investigators, *JAMA* **288**, 321 (2002).
3. D. Grady *et al.*, *JAMA* **288**, 91 (2002).

The Difficulties of Double Blinding

THE RECENT PUBLICATION OF RESULTS FROM the Women's Health Initiative (WHI) study of hormone replacement therapy (HRT) suggests that the health risks of taking HRT may outweigh the benefits ("The vanishing promises of hormone replacement," M. Enserink, News Focus, 19 July, p. 325). One interesting thing to note about HRT studies like the WHI is the strong possibility that the treatment and placebo groups can guess their assignments at a better than chance level. Beginning HRT can cause physical changes that may well be detected by women, such as a sudden reduction in hot flashes, an increase in vaginal lubrication, and mild acne. Women's guesses about their group assignment can affect their compliance with the program, as well as their choice of other treatments. It is possible that women who believe they are in the treatment group and expect HRT to help cardiovascular problems might be less likely to use the small doses of aspirin that are recommended to reduce clotting, while

Recent findings about hormone replacement therapy have left patients and doctors shaken.

others whose continuing symptoms suggest that they are in the placebo group may seek a variety of "natural" remedies for their symptoms such as soy products. A systematic effect is hard to predict, but we should keep in mind that a real double-blind design may not be possible here.

JEAN MERCER
Department of Psychology, Richard Stockton College, Pomona, NJ 08240, USA. E-mail: petedempsey@worldnet.att.net

Science and Technology Centers and Education

JEFFREY MERVIS'S DESCRIPTION OF THE SCIence and technology center (STC) program supported by the National Science Foundation (NSF) ("Science with an agenda: NSF expands centers program," News Focus, 26 July, p. 506) presents a view of the program that is not universally shared by all of the STCs. The nature of our mission, which is broad and includes not only research but also education and knowledge transfer, is demanding, but there are sufficient resources to make STCs a success. The nature of the support, up to $20 million for 5 years, with a second 5-year period of funding, allows members of our STC and others to pursue cutting-edge research that is not only high-risk but whose payoff may be years away. In coupling this commitment to education and knowledge transfer, the STCs are able to explore a complete array of science-related activities.

The article also seems to portray K-12 education as an unwelcome burden placed on the STCs by the NSF. It is suggested that individuals who direct K-12 education efforts should be drawn from the scientist pool of the university—Ramon Lopez of the Center for Integrated Space Modeling is quoted as saying "It is a mistake to put an educator in charge."

On the contrary, at the inception of the Nanobiotechnology Center (NBTC), we

gave the leadership of our K-12 program to an educator experienced in the K-12 arena, who understands the needs of schools and their populations of children and teachers and can successfully integrate the research of the center into dynamic education programs. Being a peer of the teacher provides the needed credibility where it counts.

A simple top-down translation of the scientific discoveries emanating from the research program at an STC will not necessarily attract the attention and enthusiasm of K-12 students. Our STC seeks to reach out to all students, especially minorities underrepresented in science and students who might otherwise not look at science as a career. Our Director of Education works with faculty, staff, and students of the NBTC to develop content, and it is these individuals who also visit schools, science fairs, and whatever venues allow us to pursue our mission. The NBTC mounts effective "hands-on" educational efforts that stimulate the minds of young children and encourage them to consider careers in science, math, engineering, and technology. STCs should consider the education effort as part of the overall mission of the center, equivalent to research and knowledge transfer.

CARL A. BATT*
Nanobiotechnology Center, Cornell University, 101 Biotechnology Building, Ithaca, NY 14853, USA.
*Co-director, Nanobiotechnology Center

A Bad Agenda?

JEFFREY MERVIS'S REVIEW OF 15 YEARS OF the National Science Foundation's (NSF) funding of 30 science and technology centers (STCs) ("Science with an agenda," News Focus, 26 July, p. 506) mentioned two failed centers, described "micromanagement" by NSF project monitors, and detailed the hurdles that applicants and successful center directors must overcome to receive NSF funds. It did not cite any examples of the "world-class" science and scientists that NSF purportedly supports by its multimillion dollar awards. In fact, the sole "successful STC" mentioned spent "$41 million... over an 11-year span" on establishing an earthquake monitoring system that may have practical value and even yield scientifically valuable seismic data but hardly constitutes "science" in itself.

The reason for the paucity of scientific distinction is easy to spot. World-class science comes from scientists working at their desks or in their labs, not in the halls of the NSF. Would not a better title for this review have been "An agenda without science?"

LEONID V. AZAROFF
Professor Emeritus, Institute of Materials Science, U-139, University of Connecticut, Storrs, CT 06269, USA. E-mail: leeazaroff@cs.com

CORRECTIONS AND CLARIFICATIONS

REVIEW: "The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics" by J. Hardy and D. J. Selkoe (19 July, p. 353). The review should have been accompanied by the following conflict of interest declaration: "Dr. Selkoe is a founding scientist of Athena Neurosciences, now Elan PLC, and a Director of Elan." *Science* had failed to send the disclosure form at the time the manuscript was received.

EDITORIAL: "Sharing agriculture's genetic bounty" by C. Fowler (12 July, p. 157). In the introduction of this commentary, Queen Hatshepsut was identified as the first Pharaoh of Egypt. The first Pharaoh was in fact Menes of Dynasty I. Hatshepsut was the first female Pharaoh, and she ruled during Dynasty XVIII.