

## Are apatite nanoparticles safe?

The biosafety of nanomaterials has attracted much attention recently (April 7, p 1142).<sup>1,2</sup> Surprisingly, no extensive studies have yet been done on “engineered” nanoparticles in relation to adsorption, biodistribution, metabolism, and excretion.

Calcium phosphate (apatite) deposition in soft tissue is common in inflammatory and autoimmune diseases, and is a threat for organ damage.<sup>3</sup> Yet apatite particles have recently been proposed for human use as a vehicle for vaccination, drug delivery, and stent medication. Apatite particles are also used as tissue fillers and advocated as safe and biocompatible.<sup>4</sup> However, apatite fillers frequently cause inflammation, macrophage infiltration, and the formation of giant multinucleated cells and fibrous capsules around the particles in soft tissue.<sup>4</sup>

We report here an incident in which accidental human eye exposure to biogenic nanosized calcium phosphate in the form of calcifying nanoparticles raised a strong IgG immune response against proteins

carried by the nanoparticles. The antibody titre has persisted over 10 years at a high level.

The incident occurred to a female scientist at a research laboratory in Finland in 1993. Calcifying nanoparticles, also termed “nanobacteria”, are unique self-replicating agents that deposit calcium phosphate in the size range of 100–300 nm.<sup>5</sup> They have not been fully characterised, and no data on biohazards were available at that time. Before the accident, the researcher’s serum samples were negative for both calcifying nanoparticle antigen and antibodies against calcifying nanoparticles, as measured by specific ELISA (Nanobac Oy, Kuopio, Finland). While working in the laboratory, high-pressure pipetting caused a calcifying nanoparticle pellet to splash into the researcher’s right eye. Both eyes were immediately washed with water and saline.

3 months after the accident, blood and urine samples were tested for calcifying nanoparticle cultures,<sup>5</sup> and calcifying-nanoparticle-specific ELISA and blood cell counts were done. Blood cell counts were normal, and calcifying nanoparticles antigen

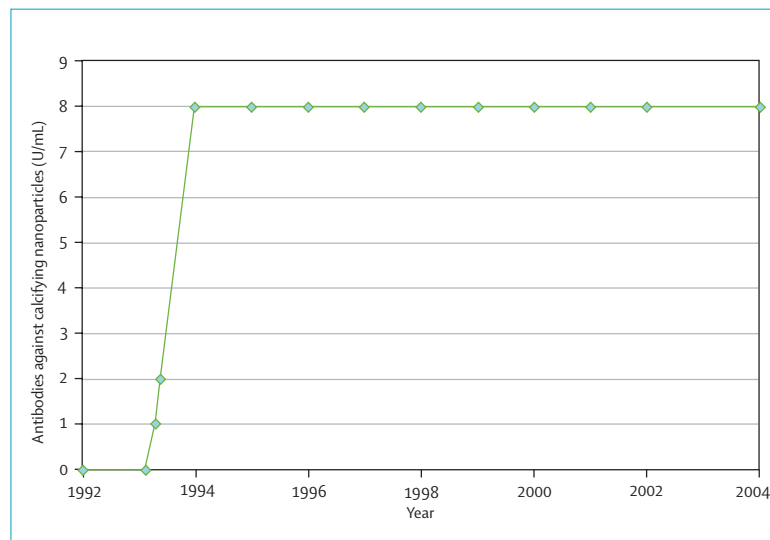
and culture tests were negative. However, a high IgG antibody titre against calcifying nanoparticles was detected (figure). The researcher’s antibodies have been used since as a positive control and standard in ELISA manufacturing (Nano-Sero IgG ELISA, Nanobac Oy, Kuopio, Finland). Studies are needed on the mechanisms of these potentially pathogenic particle-mediated immunological reactions. Because of this researcher’s documented strong immune response against calcifying nanoparticles, we recommend testing and caution before using fine-grained apatite in applications requiring insertion into the human body.

Nanobac Pharmaceuticals is the manufacturer of the ELISA kits used in this research. NC and EOK own stocks in that company.

\**Neva Ciftcioglu, Katja M Aho, David S McKay, E Olavi Kajander*  
neva.ciftcioglu-1@nasa.gov

\*NASA Johnson Space Center, Houston, TX 77058, USA (NC, DSM); University of Kuopio, Kuopio, Finland (KMA, EOK); and Nanobac Pharmaceuticals, Tampa, FL, USA (NC, EOK)

- 1 The Lancet. The risks of nanotechnology for human health. *Lancet* 2007; **369**: 1142.
- 2 Bergamaschi E, Bussolati O, Magrini A, et al. Nanomaterials and lung toxicity: interactions with airways cells and relevance for occupational health risk assessment. *Int J Immunopathol Pharmacol* 2006; **19** (suppl 4): 3–10.
- 3 Dalbeth N, Haskard DO. Inflammation and tissue damage in crystal deposition diseases. *Curr Opin Rheumatol* 2005; **17**: 314–18.
- 4 Marmor ES, Phelps R, Goldberg DJ. Clinical, histologic and electron microscopic findings after injection of hydroxyapatite filler. *J Cosmet Laser Ther* 2004; **6**: 223–26.
- 5 Kajander EO, Ciftcioglu N. Nanobacteria: an alternative mechanism for pathogenic intra- and extracellular calcification and stone formation. *Proc Natl Acad Sci USA* 1998; **95**: 8274–79.



**Figure:** Follow-up of laboratory worker’s antibodies against calcifying nanoparticles during 12 year-follow-up

Conjunctival pouch exposure to calcifying nanoparticles occurred at 60 months. The ELISA test is done for a serum dilution of 1:500. Measuring range is 0–8 U/mL and values >8 U/mL are presented as 8.

### Department of Error

*Wong T, Mitchell P. The eye in hypertension. Lancet* 2007; **369**: 425–35—In this Review (Feb 3), the name of the first author should have been Tien Yin Wong.

*The Lancet. DFID’s health strategy. Lancet* 2007; **369**: 1973–74—In this Editorial (June 16), the second sentence of the third paragraph should have read: “For instance, it is already largely agreed that many if not most of the Millennium Development Goals will not be met.”