Great balls of fire: How heating up testicles with nanoparticles might one day be a form of male birth control

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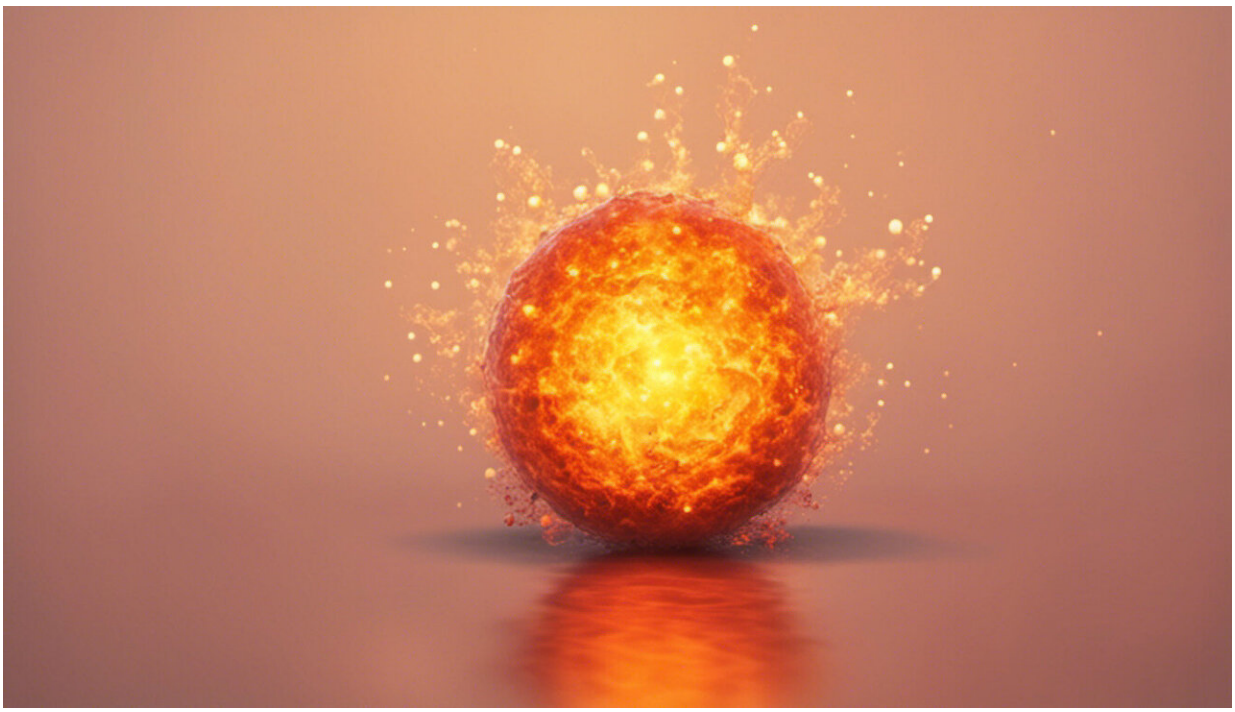

Credit: AI-generated image (disclaimer)

Women have a variety of methods for contraception, but only two methods are commonly available to men: condoms and vasectomies. Both methods have their drawbacks.

Condoms can break, and some men are allergic to the latex in standard condoms. Vasectomies are surgical procedures that can be painful and difficult to reverse.

So the search for alternative male contraceptive options continues, and one method currently being investigated is nanocontraception.

An on/off switch

Nanocontraception is based on the idea that nanoparticles—here, about 100 nanometres in diameter, or roughly one-thousandth the width of a piece of paper or of a strand of human hair—can somehow be delivered to the testicles, where they can be warmed.

If you could warm up the testicles just a bit, you would have a way to turn sperm production on and off at will because the warmer they get, the less fertile they become. But it's a delicate process because the testicles can be irreversibly destroyed if they become too warm; the tissue dies and can no longer produce sperm, even when the testicles return to their normal temperature.

Using nanotechnology to warm testicles was first studied in 2013 on mice by biologist Fei Sun and his multidisciplinary research team. His early experiments involved injecting nanoparticles directly into mouse testicles. These nanoparticles were long nanorods (or nanocylinders) of gold atoms—imagine a tube 120 gold atoms long with a diameter of 30 gold atoms—coated with a few long polymer chains on their surface. They looked like oblong bacteria with hairs sticking out.

Infrared radiation was then used on the mice's testicles. This caused the nanoparticles to warm from around 30 C to between 37 and 45 C. The exact temperature depended on both the concentration of nanoparticles injected and the intensity of the radiation.

The radiation caused heat lesions on the skin surrounding the mice's testicles, so it was assumed that this procedure was painful for the animals, even though there was no reliable way to measure their pain. The researchers decided to look for other ways to inject the nanoparticles.

Iron rods

In July 2021, Sun's team published a paper on their latest findings. The nanorods in the new method are composed of magnetic iron oxide instead of gold, and they are coated with citric acid instead of ethylene glycol—but they have the same size and shape as the earlier nanorods.

These magnetic nanoparticles were injected into mice's veins, and then the animals were anesthetized. A magnet was then placed next to their testicles for four hours, drawing the nanoparticles there.

This procedure—injection followed by magnetic targeting—was performed daily for one to four days.

After the last day of treatment, an electric coil was wrapped around the testicles, through which a current was passed. This induced a magnetic field that heated up the nanorods and, therefore, the testicles. Similar temperature increases—from a baseline of 29 C to between 37 and 42 C—were observed through this method. The more days a mouse had been injected with nanorods, the hotter its testicles became.

Credit: AI-generated image (disclaimer)

Hotter testicles led to their atrophy and shrinkage, but they showed gradual recovery both 30 and 60 days after treatment as long as testicle temperatures didn't reach 45 C. Fertility was down seven days after treatment—in some cases, fertility was completely eliminated—but it also showed gradual (though not complete) recovery after 60 days.

Although fertility was not back to normal levels, there was no noticeable difference in the litter size of females impregnated by the treated mice and no morphological defects were observed in any of the mice pups. There seemed to be no difference in the sperm that did make it through.

And Sun and his colleagues found that, unlike the gold nanorods that stayed indefinitely in mouse testicles, the iron nanorods were gradually eliminated into the liver and spleen, and later fully eliminated from the

body. This reduced the risk for long-term toxicity.

Controlled breeding

The cost and the irreversibility of surgical castration lead many pet owners to look for alternative methods of contraception. Nanocontraception is ready to be used on household pets, says Sun, and adds that this method is already being used on cats in China.

Surgical castration is less popular in Europe than in North America, so nanocontraception might be of greater interest there, says David Powell, director of the Reproductive Management Center of the Association of Zoos and Aquariums in St. Louis, Mo. "There's really not a big pet contraception market in the U.S.," says Powell.

He adds that contraception is not typically used with agricultural animals like sheep and cows. "They are reared for consumption and slaughter, so the agriculture industry is not doing much, if any, research on animal contraception."

"Zoos are a very small market, and so drug companies don't have a lot of motivation to make animal contraceptives," says Powell. But some of them do, and the Reproductive Management Center collects data to evaluate how contraceptives work on different species.

Nanocontraception could be a part of zoos' reproductive toolkit one day. But before this happens, says Powell, further studies would need to establish how painful it is and in which species the iron nanorods can be used. Research has indicated that some mammals—such as rhinoceroses, lemurs and dolphins—might accumulate iron, which can be toxic in larger quantities.

Reversible options

One potential advantage of nanocontraception is its reversibility, as zoos often try to precisely time breeding events over animals' life cycles. But just how reversible it is needs further study. All of Sun's experiments treated mice only once; they were never subjected to a second injection of nanoparticles after their testicles had healed.

Sun's ultimate goal is human contraception, although he admits that's still a long way off. As with zoo animals, detailed studies will be required to establish that nanocontraception is not toxic for men. It is also more difficult to put a man under anesthesia for four hours and wrap an electric coil around his testicles than it is to do the same thing on a mouse. Instead, Sun hopes to be able to deliver the magnetic nanorods orally and find another way to direct them to the testicles.

And it is uncertain how many men will be comfortable with shrunken testicles, even if they recover their original size with time.

Until then, better get those condoms out.

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