REVIEW of Ophthalmology

Vol.13:Issue11 November 1, 2006: Pages 31-34

Very Small May Soon Become Very Big

Nanotechnology may seem like the musings of H.G. Wells, but it may well change the way we treat diseases.

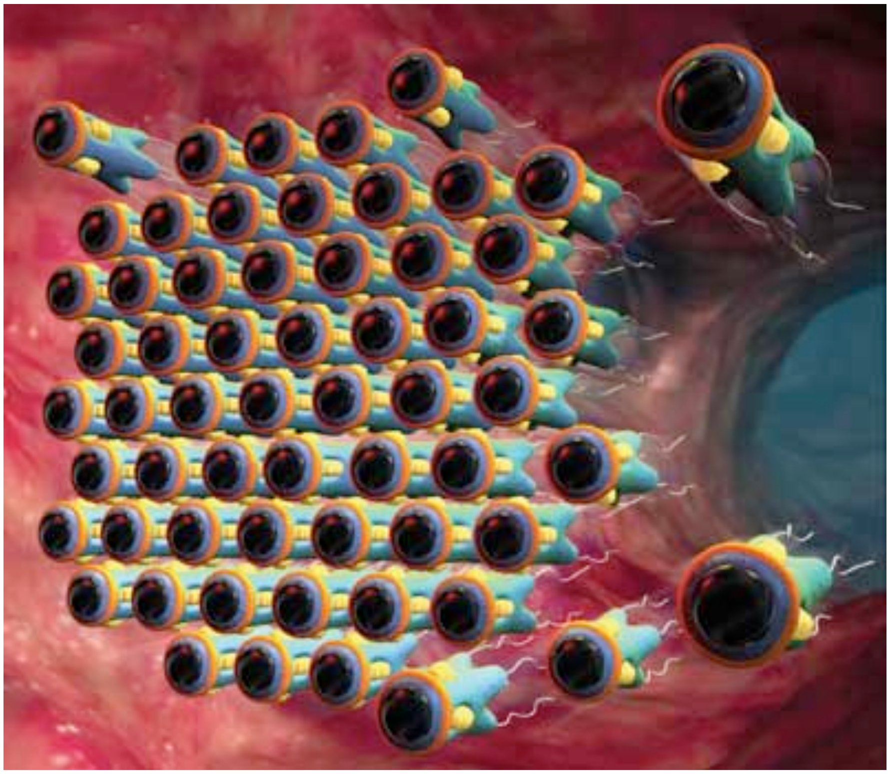
Robert M. Kershner, MD, MS, FACS, Boston

If you haven't heard about nanotechnology—the creation of ultra small particles—you are about to. This field of atomic science is red hot, and the technology it is spawning is showing up practically everywhere. From cosmetics that can be spread on the skin to capture the vitality of youth, to household products that keep themselves clean, nothing is off limits for this incredibly small technology. These tiny particles are poised to forever change the way we think, how we eat, what we purchase, and how we will practice medicine.

Medicine is on the verge of something really big, or actually, very small. What was formerly called "micro," is not small anymore. To be really small, a particle has to be at least one billionth of a meter (10^{-9} m), much smaller than 80,000 nanometers or the thickness of a human hair. Things this size are called nanoparticles. They have properties that can be exploited to keep clothes clean, improve food packaging, create new pharmaceuticals that carry life saving drugs into unreachable places, and produce micro medical devices that are capable of performing atomic surgery. Sound unbelievable? The earliest fruits of this research are about to enter into clinical practice this year.

The science that makes this all possible exists on a quantum/atomic scale. By varying the structure and composition of common materials, scientists can dramatically change their physical, chemical and biological properties. These miniscule nanoparticles can travel freely through the blood stream to target a specific cancer or can be placed in an eye drop to treat glaucoma.

According to the National Nanotechnology Initiative, the U.S. government will spend more than $1.05 billion on nanotechnology this year alone. Most scientists agree the money is well-spent. The National Science Foundation has funded the National Nanotechnology Infrastructure Network (NNIN) comprising 13 university sites that form a nationwide system of research and education centers devoted exclusively to nanoscale science, engineering and technology. A look at the research already under way is breathtaking.



Computer artwork of units for a nanotechnology camera inside the human body. Each unit provides part of the picture, similar to the compound eyes of insects. The units are also a light source because they are bioluminescent. The small size allows the individual units to view any area of the body without requiring an operation. The picture is assembled from images beamed back to a receiver. This is an example of the future development of microscopic technology for novel uses.
Photo Researchers Inc.

Consumer Products

Imagine packaging material that actually prevents spoilage of the food it contains. Or a cutting board impregnated with nanoparticles that make it impossible for food particles and bacteria to adhere to its surface. One rinse with water and the surface is once again sterile. Nanoparticles are being applied to the next generation of textiles, making clothing stain-proof and the crease on your pants truly permanent. Diapers that don't smell? Ties that need only to be shaken to remove a stain? Don't disparage the concept; the products are already on their way to a store near you.

The Japanese, who have long had an interest in a manufacturing a more hygienic toilet and making it your own personal spa, are finally reaching their goal. By coating a special porcelain-like material with nanoparticles they have created a toilet that will not allow organic material, bacteria or viruses to attach themselves. Throw away your cleansers and brushes—this commode does it all. Now if we could only do the same with people's hands … .

Medical Applications

Scientists at Renssalaer Polytechnical Institute have created organic gel nanomaterials that can encapsulate pharmaceutical, food or cosmetic products. With this technology virtually any substance could be made into a topical cream. Nanotechnology is being applied to create faster and more cost-effective medical machines. At the University of North Carolina at Chapel Hill computed tomography images have been created with carbon nanotube X-rays.

Quantitative imaging of cells is an important tool for the diagnosis of cancer and for measuring the amount of a chemotherapeutic agent that is actually delivered to individual cancer cells. A novel chemical nanotransistor makes it possible to create ultra sensitive bio-medical devices that can detect a single-antigen in a blood sample or a single cancer cell. A nanoparticle-based drug delivery system in which an applied magnetic field directs the accumulation of drug-filled nanocarriers into tumor cells was recently published in *Molecular Pharmaceutics*. And silver and gold, precious metals that are key ingredients of nanocomposites, can be designed to measure the actual amounts of drugs being absorbed by cancer cells, according to the results of a study published in *NanoBiotechnology*.

Of all the successes to date, it may actually be the failures that make the greatest contribution. Ever since the completion of the mapping of the entire human genome several years ago, there has been a lot of excitement surrounding the creation of gene-directed therapies. What is less well-known about this concept is that conventional gene therapy has had few successes to date. Finding a suitable means of transporting a nucleic acid "drug" into a diseased target cell has been seemingly impossible. Typically, heat-killed viruses have been used as “taxis” but with little success. Nanoparticles could fill the role. Attaching large molecules to small particles could make targeting and penetration of complex gene segments as simple as point, aim and shoot.

Creating replacement parts for an aging population is a daunting task. Using nanotechnology, building 3-D biological scaffolds for the next generation of tissue engineering will be as commonplace as growing fruits and vegetables. The intriguing concept of shape-memory polymers will finally be arriving in medical clinics this year. These materials transform themselves into a pre-determined shape when activated by light, heat or a magnetic field, and they can be implanted and activated anywhere in the human body. The first of these technologies will appear in the form of self-tying sutures and fast-adjusting orthodontic braces. There are many more on the horizon.

Ophthalmic Applications

According to Rutledge Ellis-Behnke, PhD, a brain and cognitive sciences researcher at MIT in Cambridge, Mass., the optic nerve could be regenerated with nanotechnology. His research team cut the visual pathways in the brains of small lab animals, resulting in blindness. They then injected a suspension of critical amino acids into the damaged area. These polypeptides, by binding to one another, assembled into nano-scale fibers that bridged the gap left by the damage. Scar formation was prevented and cell growth was able to occur. Approximately 30,000 nerve cell connections were restored in each case, allowing 75 percent of the animals to see well enough to detect and turn toward food.

Nanotechnology may make non-compliance with drug delivery a thing of the past. Imagine if all a glaucoma patient would have to do for a month’s treatment was to place a contact lens on the eye. The idea, of course, is nothing new, but nanotechnology may finally make it work. Scientists at the University of Florida fabricated hydrogel contact lenses seeded with drug-laden nanoparticles. Once placed on the eye, a passive diffusion gradient releases the molecules from the nanoparticles into the eye. Plans are under way to test timolol (Timoptic). “Other researchers have tried to use contact lenses for drug delivery, but our approach is novel and has never been tried before,” says Anuj Chauhan, MD, of the UF research team.

The precious metals previously mentioned could prove to be precious indeed. Billions of gold nanoparticles could be placed in a single eye drop and then applied topically to treat glaucoma. Once inside the eye, activating the gold nanoparticles within the trabecular meshwork using a Titanium-Sapphire infrared laser could permanently open clogged drainage channels. Crystalline silver nanoparticles are already available as antimicrobials in dressings and newer topical forms could make ocular infections a thing of the past.

One of the more exciting additions to the new emerging field of vascular endothelial growth factor inhibitors may be the intravitreal delivery of these potent molecules by piggybacking them onto nanoparticles. Having free access into the eye from outside the eye wall will virtually eliminate the need for a needle and intraocular injections.

All that glitters is not gold, or silver, however. Behind these promising new technologies lurks an unforeseen downside risk. The human body's normal defense against foreign invaders—skin, mucus membranes of the eyes, nose, throat, lungs and intestine—could be rendered useless by invisible particles that pass freely through biological membranes. The nose, usually the first line of defense against inhaled airborne particles that could damage the lungs, may itself be susceptible to the dangers of extremely small nanoparticles. The implications of possibly unforeseen consequences of this ultra small technology remain to be seen. Maybe they won't be a big thing.

Dr. Kershner is president of Eye Laser Consulting. He has no financial or proprietary interest in any of the technologies described in this article. For more information on nanotechnology visit nano.gov.