Halting The Medical Device-To-Infection Connection

Breakthrough Technology Offers Safe, Cost-Effective Means of Rendering Virtually Any Medical Device Free from Biofilm Formation

by Jack Rubinger

What if medical devices were protected from bacteria—if the actual plastic, metal, silicone and other materials that made up the device were impervious to germs? What if the surface of catheters, heart monitors, artificial joints, intravenous tubes and virtually any other medical device were made inhospitable to biofilm and resistant to the transmission of infections?

According to research numbers from the Centers for Disease Control and Prevention (CDC), controlling hospital-acquired infections would help prevent millions of medical complications and save thousands of lives each year. It would also save hospitals billions of dollars in reduced medical costs. The Committee To Reduce Infection Deaths (RID) estimates that hospital-acquired infections add $28 billion to $30 billion to the nation's health costs each year.[1] Because insurance companies do not usually cover costs outside of the patient's original condition, billions of dollars in related expenses are passed on to the hospitals themselves.

While studies conclude that the first line of defense against nosocomial infections includes the enforcement of hand washing and other Universal Precautions, research also indicates that a significant number of hospital-acquired infections are transmitted via indwelling medical devices.[2] Halting the medical device-to-infection connection could, therefore, have a significant impact on reducing the instances of nosocomial infections.

A recent breakthrough in antimicrobial technology offers real hope for advancement in this effort. A new medical device treatment technology called SilvaGard™ uses a uniquely flexible and effective form of antimicrobial silver to render medical devices impervious to bacteria. Through a simple dipping process, device manufacturers can easily and cost effectively add antimicrobial properties to their products.

Best of all, the technology is more than a dream for the future. Its first application has already gained FDA approval, and products that incorporate its use were made available on the market late last year.

The Search For A Better Medical Device Treatment

The medical industry has long sought an effective and practical way to protect indwelling devices from bacteria. To date, the methods used fall into two broad categories: direct incorporation and coating.

Direct incorporation is a process that adds the bacteria-killing agent directly into the raw materials that are then used to manufacture the medical device. The surface of the finished product, therefore, contains small amounts of antimicrobial particles that help kill bacteria.

This method has several drawbacks. First, it can only be used in nonmetallic products—primarily plastics that are thermoformed or polymerized during the manufacturing process. This eliminates its possible use for thousands of other medical devices for which infection control is critical. Secondly, since the antimicrobial agent is added into the actual material of the device, it can change the property of that material, making it less suitable for its original application. This can lead to costly reengineering and redesign costs. Since only the antimicrobial agent that makes it to the surface of the finished materials serves its purpose, most of it is wasted. This can affect the product's final cost.

Coating a finished medical device with an antimicrobial substance involves electroplating (metal surfaces), sputter coating (plastics) or "painting" the outside of the product using processes that adhere antimicrobial agents to its surface. While this may be effective in some applications, it, too, has drawbacks.

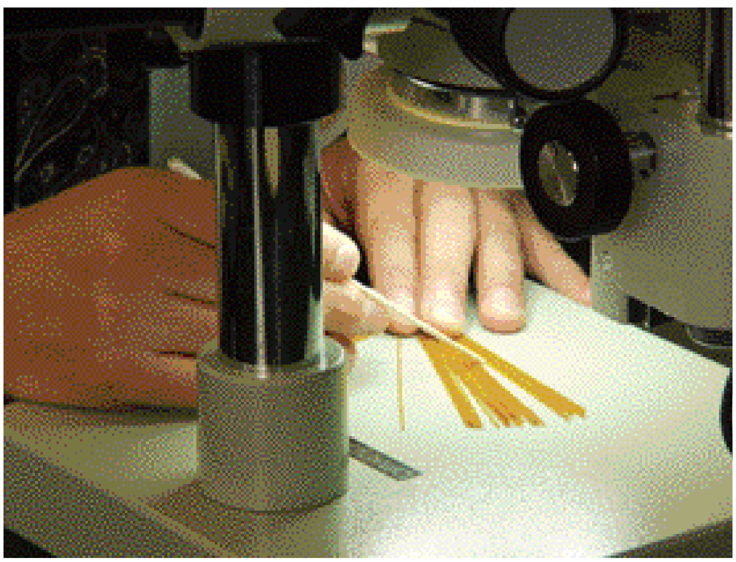
Coatings often change the properties of the device—clogging holes, making it thicker or less flexible, and, therefore, unsuitable for its originally intended purpose. Some devices are simply unsuitable for coating because the antimicrobial spray is unable to reach all surfaces. Coating can easily cover the outer surface of a catheter, for instance, but it's much more difficult to cover the interior of the device. Some coatings can also flake or break off of the device's surface, leading to other complications.

A Breakthrough Process

SilvaGard, an antimicrobial technology developed by AcryMed Inc., a leading infection control and wound care technology company, is neither a coating (on top of the surface) nor a direct incorporation (in the material) process. Instead, it is the creation of silver nanoparticles on the surface of the medical device.

The SilvaGard treatment is a relatively straightforward "dipping" process where the entire surface of the device is immersed into a liquid solution containing silver nanoparticles. This allows all exposed surfaces to come in contact with the antimicrobial agent. As the device is dipped into the solution, the silver nanoparticles form on its surface. The device is then removed, rinsed thoroughly, and dried.

The silver nanoparticles adhere so strongly to the device that they remain attached even after ultrasonic cleaning. This is true no matter what material is being treated (Figure 1). In fact, research has shown that SilvaGard tenaciously adheres to Teflon® and other "stick free" substances. When used on elastic devices, the antimicrobial silver remains firmly on the device even after stretching or flexing.



AcryMed scientists take a closer look at catheters treated with SilvaGard, a silver antimicrobial nanotechnology for medical devices.

Example Materials Treated

Glass	Rayon	Nylon
Stainless Steel	Polyester	Silicone
Polyproplylene	Silicon	Polyimide
Polyethylene	Titanium	PEEK
Polyurethane	Ceramic	PTFE
Cotton	Polysulfone	Polycarbonate

Figure 1.
SilvaGard proved to tenaciously adhere to the surface of virtually all materials tested.

The tiny amount of silver nanoparticles deposited onto the device is controlled by adjusting the silver concentration, the temperature of the dipping solution and the amount of time the device is left in the SilvaGard solution. Since the particles are so small and attach to the submicroscopic nooks and valleys of the device material, they do not change the dimensions or physical characteristics of the product. (The size of these silver nanoparticles is about 10 nanometers—a bacterial cell is typically between 1,000 to 3,000 nanometers in size).

More importantly, the SilvaGard treatment provides a safe, highly effective antimicrobial protection to the device.

Safe, Effective, Sustainable Protection

Medical science has discovered that the infections that threaten patients treated with implanted and indwelling medical devices are caused by the formation of biofilms on the surfaces of the device. Biofilms are formed when fast mutating versions of individual, free-floating bacteria attach to a surface where they multiply, colonize and form a polysaccharide covering that protects the bacteria colonies.[3] Biofilms are very difficult to remove and can result in serious bloodstream infections, organ failure and death. They also protect the bacteria underneath, allowing them to emerge days, weeks or even months after they've been introduced into the body.

The key to preventing biofilms is to prevent the individual planktonic bacteria from colonizing on the surfaces of medical devices. Silver has proven to be a particularly effective surface treatment for this purpose.

Unlike antibiotics, which are designed to fight a specific microorganism, ionic silver has a mechanism that simultaneously attacks multiple sites (up to 10) in the cell. Pathogenic cells cannot mutate fast enough to avoid the multiple attacks. As a result there are no known silver-resistant bacteria among medically relevant strains. It is this property that has caused infection control doctors, surgeons and wound care specialists to value silver technology for medical devices to prevent and lower infections.[4]

Studies show that depositing silver on medical device surfaces can prevent biofilm formation across a broad spectrum of pathogens including *Staphylococcus aureus, E Coli, Pseudomonas aeruginosa, Enterococcus sp*, and *Candida albicans,* to name a few. Figure 2 shows how SilvaGard effectively prevents the formation of biofilms of five separate medically relevant microbes on the surface of a treated catheter. The optical density reading for the treated device was, in all cases, at or below the background or "Control" reading, which indicates no growth of biofilm.

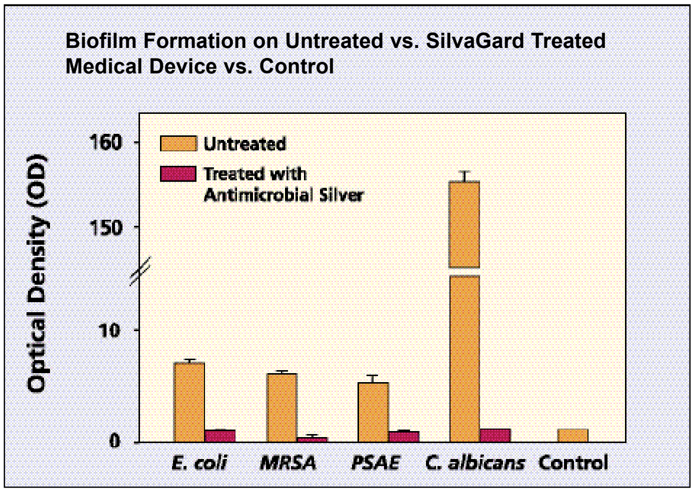


Figure 2. SilvaGard effectively prevents the formation of biofilms of five separate medically relevant microbes on the surface of a treated medical device.

Unlike traditional coatings that leave many areas of a device unprotected, SilvaGard's dipping process ensures that all exposed surfaces are covered. This includes hard-to-reach places such as inside devices and the lumen of catheters.

SilvaGard's infection-fighting properties can last days or months or more depending upon the device application. The period of efficacy can be varied by altering the amount of silver applied to the device during the treatment process. This allows device manufacturers to customize the process in order to best meet specific requirements. For example, a device that resides in tissues for only a few days would need a lower loading than a permanently implanted device.

SilvaGard is also safe. Ionic silver is oligodynamic, which means it is effective at very low doses—as low as 0.001 ppm. Although silver is a heavy metal, in these very small amounts it is nontoxic to human cells and, therefore, very safe.

Biodistribution research also shows that ionic silver from treated devices is not accumulated in any organs in the body. In a to-be-published study conducted at Oregon Health and Science University (OHSU), researchers traced the spread of radioactive silver applied

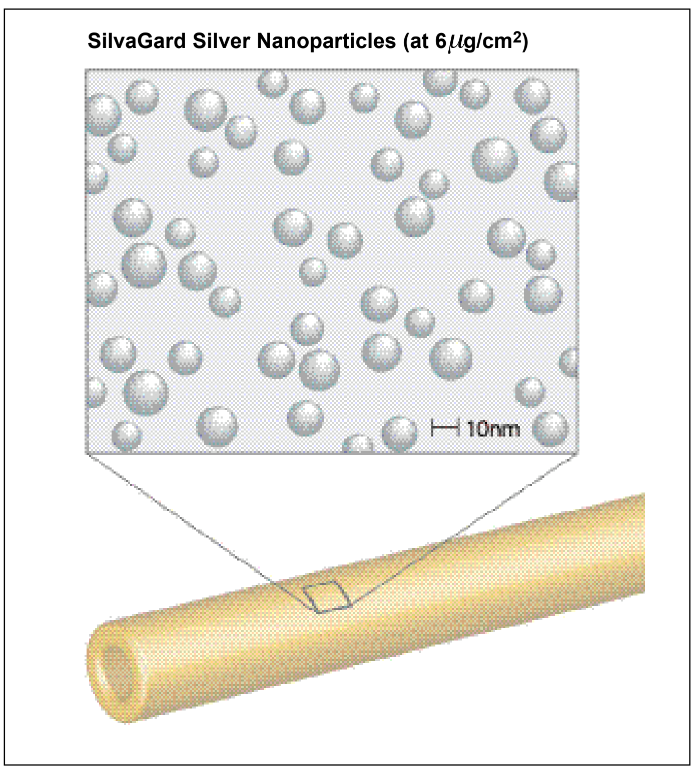


Figure 3. SilvaGard's silver nanoparticles are shown attached to the surface of a medical device.

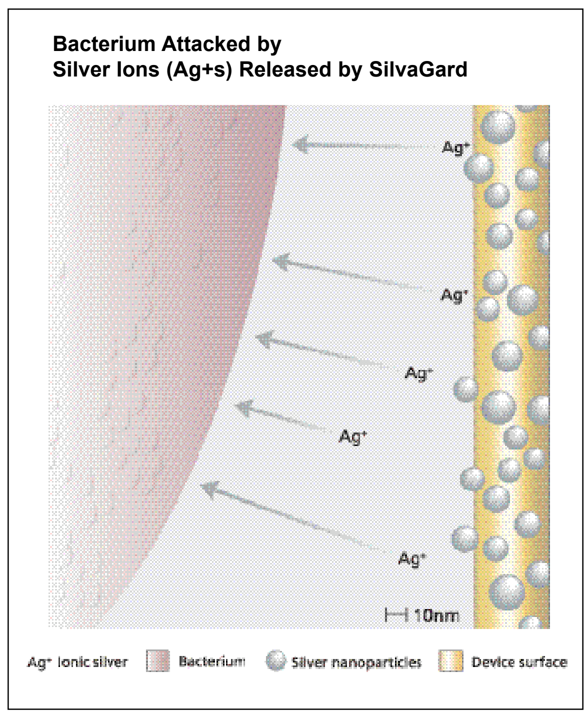


Figure 4. Because of the silver nanoparticles, the bacterium on the left (large by comparison—4 to 5,000nm) cannot adhere to the surface of the medical device to form a biofilm.

to catheters implanted in laboratory mice. After a 10-day period, researchers found that all but an insignificant amount of silver remained on the catheter and in the tissue pocket, or was eliminated through fecal waste. The silver used in SilvaGard technology also elutes such small amounts of silver that there should be no negative interaction with drugs.

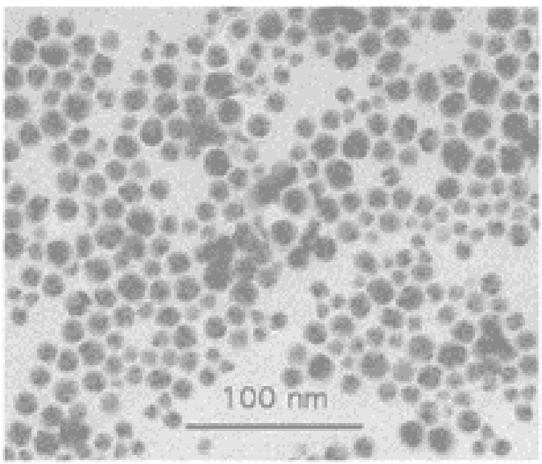


Figure 5. This shows the uniform discontinuous deposition of nanoparticles on the material surface.

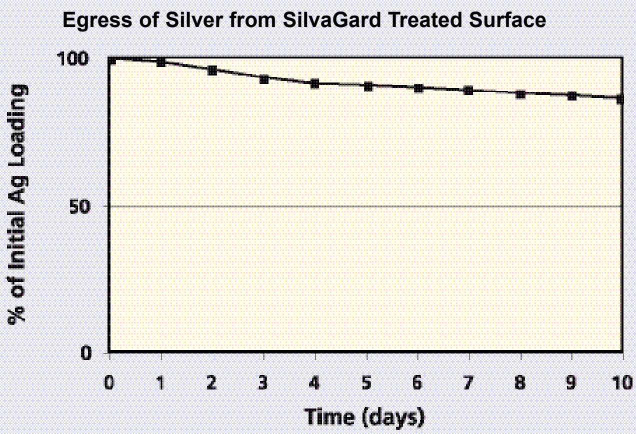


Figure 6. Graph shows sustained release of silver from a treated device. The elution rate of silver from this device treated with approximately 8.0 μg/cm^2 predicts a release sustained for 150 days.

FDA Approvalwhch

Toward the end of 2005, the FDA granted approval for the first use of SilvaGard technology. The initial clearance was given to I-Flow Corporation for marketing the company's ON-Q, SilverSoaker™ regional anesthesia delivery catheters. I-Flow has since begun incorporating the SilvaGard treatment into the production process of its SilverSoaker catheters, and the devices were introduced to the market late last year.

Since its initial introduction, SilvaGard has gained the attention of device manufacturers representing a large spectrum of medical products from heart monitors to catheters.

The high rate of hospital-acquired infections is a serious problem affecting millions of patients each year. Every person entering a U.S. hospital today has a one in 20 chance of contracting an infection unrelated to the illness or injury for which they entered. The average cost of treating an infection is $14,000 to $15,000. The cost of treating a more serious bloodstream infection can average as much as $57,000.[1]

Most of these infections are preventable. A majority are transmitted to patients via medical products—particularly indwelling and other percutaneous devices. And while there are several traditional methods used by device manufacturers to limit the spread of bacteria through their products, they have limitations. Some are costly or require manufacturers to completely redesign their products. Others work only on certain materials, and their effect on reducing the spread of bacteria may be limited.

SilvaGard represents the first real breakthrough in years that offers a significant alternative to the infection control treatments available to medical device manufacturers today. SilvaGard technology can be used on virtually any medical device. It is a relatively simple, cost-effective process that can be added to most any existing manufacturing process. SilvaGard doesn't change the physical characteristics of the medical device being treated or alter its functionality. Most importantly, SilvaGard is a safe and highly effective way to transform medical devices into antimicrobial products that can help halt the spread of nosocomial infections. ✢

References

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3. R.M. Donlan. "Biofilms: Microbial Life on Surfaces," Emerging Infectious Diseases, vol. 8, no.9, Sept. 2002.
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