RESEARCH ADVANCES
Blue Light May Deserve Green for Treating Skin Infections
David C. Holzman

Blue light selectively eradicates *Pseudomonas aeruginosa* on the skin and in infected soft tissues without harming host cells, according to Michael R. Hamblin of the Massachusetts General Hospital (MGH) and Harvard Medical School (HMS) in Boston, Mass., and his collaborators. If this approach proves safe and effective, blue light could become a nontoxic means for treating burn or other patients, who are prone to infections with *Pseudomonas*, including drug-resistant strains. Details appear in the March 2013 *Antimicrobial Agents and Chemotherapy* (57:1238–1245).

This use of blue light is by no means the first time light was evaluated as a means for treating infections, according to Hamblin’s collaborator Tianhong Dai. Other approaches, including antimicrobial photodynamic therapy and ultraviolet-C (UVC) irradiation, can be effective alternatives to conventional means for treating skin and soft tissue infections “regardless of antibiotic resistance,” he says. However, photodynamic therapy is complicated by the need to use photosensitizers. This addition can be difficult in itself, but also can inadvertently introduce the photosensitizers into host skin cells, making them more vulnerable to UVC than they already are, narrowing the therapeutic window.

However, blue light kills bacteria without reliance on photosensitizers and, by itself, is nontoxic to mammalian cells. Yet, its effectiveness against bacteria was not adequately tested before nor fully appreciated, according to Dai. “There have been—rather surprisingly—no published reports to demonstrate blue light therapy for skin and soft tissue infections,” he says.

Blue light apparently targets porphyrin molecules that are found in bacterial cells but not mammalian cells, Dai continues. Thus, *P. aeruginosa* is 35 times more sensitive than are human keratinocytes to blue light. In another experiment, all the *P. aeruginosa*-infected mice survived following blue-light treatment, whereas 9 of 11 of the infected but untreated mice died.

“The results demonstrating the reduction in wound infection and prevention of lethal bacteremia in mice are groundbreaking, and highlight the potential for this technology in wound disinfection treatment,” says Michelle MacLean of the University of Strathclyde in Glasgow, United Kingdom. “Clinically, I use blue light with wounds and see consistently good outcomes, but strong research on in vivo models is lacking,” adds James Guffey of Arkansas State University, Jonesboro. “This is a real addition to the literature.”

Skin and soft tissue infections are the second most common bacterial infections encountered in clinical practice, according to Hamblin. “The prevalence of skin and soft tissue infections among hospitalized patients is 10%, with approximately 14.2 million ambulatory care visits in the United States, and an annual associated medical cost of almost $24 billion,” he says. “Treating resistant skin and soft tissue infections often requires the use of more expensive or more toxic drugs and can result in longer hospital stays for infected patients.”

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SCIENCE POLICY
GAIN Act Asks FDA To Identify Priority Pathogens
Jeffrey L. Fox

In response to mandates in the Generating Antibiotic Incentives Now (GAIN) Act of 2012, officials of the Food and Drug Administration (FDA) are identifying “qualifying pathogens” to be the designated targets for new antimicrobial drugs. The GAIN law, which took effect late in 2012 as part of FDA reform legislation, offers incentives to those developing such drugs, including extended market exclusivity and fast-track regulatory reviews. Based on an early round in this pathogen-naming effort, agency officials will face a challenge in keeping that list of

Blue light may be a safe and effective way to treat *Pseudomonas* skin infections, lessening the need for drugs and potentially shortening hospital stays for many patients (Photo © Krzysztof Zmij/iStockphoto.)
MINITOPI

Recent Developments Touching on Antibiotic Resistance

Several recent developments that touch on antibiotic resistance include:

- In a February 2013 report, “Countering the Problem of Falsified and Substandard Drugs,” from the Institute of Medicine in Washington, D.C., committee members emphasize that substandard versions of antimicrobial drugs, particularly in poor countries, can induce and are “driving” the development of drug resistance globally. Details are available: http://www.iom.edu/Reports/2013/Countering-the-Problem-of-Falsified-and-Substandard-Drugs.aspx.

- Antibiotic use on farms in China is not monitored but as many as 149 antibiotic resistance genes can be detected in manure from such farms, according to James Tiedje of Michigan State University in East Lansing and his collaborators. Details appear in the February 11, 2013, Proceedings of the National Academy of Sciences (doi:10.1073/pnas.1222743110).

- In response to expanding drug resistance, the German National Academy of Sciences Leopoldina of Berlin, Germany, in January issued a report, “Antibiotic Research: Problems and Perspectives,” containing eight recommendations to prevent further spread of resistance and to develop novel antibiotics. For details, see http://www.degruyter.com/doi:10.1515/jfd.2013.60.

- Nicking enzyme plays a key role enabling plasmids carrying drug resistance genes to spread from one strain of Staphylococcus aureus to another, according to Matthew Redinbo of the University of North Carolina at Chapel Hill and his collaborators. Details appear in the January 28, 2013 Proceedings of the National Academy of Sciences 10 doi.1073/pnas.1219701110.

- The bacteria associated with ornamental fish carry high levels of resistance to a wide range of antibiotics, according to Tim Miller-Morgan of Oregon State University in Newport and his collaborators. Details appear in the January 2013 Journal of Fish Diseases (doi: 10.1111/jfd.12044).

Pathogens from becoming all-inclusive. Indeed, some experts argue that the more expansive the list becomes, the better.

As part of this priority pathogen-identifying effort, FDA officials convened a hearing last December near Washington, D.C., inviting experts to share their views on which pathogens deserve special attention and to address whether the agency’s underlying rationale makes sense. Initially, several familiar pathogens were put forth as “posing serious threats to public health” and thus worthy of being on the list, including methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), multidrug-resistant (MDR) gram-negative pathogens, and MDR Mycobacterium tuberculosis.

No one seems to quarrel with those choices for the roster. However, few experts resisted adding to the list during the December gathering, a response that could signal an early exponential expansion phase. Here is how several participants suggested that the list should grow.

One set of additions would be pathogens that cause havoc among hospital patients, such as Klebsiella and Clostridium difficile and also drug-resistant Candida species along with other pathogenic fungi, according to Amanda Jezeck of the Infectious Diseases Society of America in Arlington, Va. She also recommends Neisseria gonorrhoeae—an addition that William Smith, executive director of the National Coalition of STD Directors in Washington, D.C., endorses. “We are moving toward untreatable gonorrhea,” he says. “It’s frightening, the drug pipeline is running dry, and new treatments are necessary.”

Other experts urged adding other pathogens. Streptococcus pneumoniae belongs on the list, says Prabhavathi Fernandes of Cempra Pharmaceuticals in Chapel Hill, N.C., pointing to its resistance to an expanding number of antibiotics. Similarly, Renu Gupta of Insmed in Monmouth Junction, N.J., calls on the agency to include the M. avium complex as well as several other mycobacterial species that, she argues, “cause significant morbidity and mortality” and, in the United States, are “far more common than tuberculosis.”

Several other experts encourage FDA officials to be “inclusive” with pathogens because now-effective drugs likely will falter when used to treat patients with such infections in the near future. “Consider a global focus” and include pathogens that pose “serious or life-threatening diseases where there are few treatment options,” says Erin Duffy of Rib-X Pharmaceuticals in New Haven, Conn. She also points to “biothreat” agents as well as MDR Escherichia coli, for which antibiotics are available but are cumbersome to administer to patients.

“The list should be inclusive, and [FDA] should consider additions as often as necessary,” agrees Barrett Thornhill, who directs the Antimicrobial Innovation Alliance in Washington, D.C. The broader its reach, he adds, “the more helpful it will be to industry and investors.”

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