
Evaluating self-collected samples was a critical milestone towards enabling same-day screening and treatment, which is needed in high-burden, low-income countries such as Papua New Guinea, Vallely says. When such patients leave clinics, typically it becomes difficult or impossible to find them again for follow-up treatments. “The majority of the country’s population lives in rural communities, many of which are very isolated,” he says. Few roads, difficult terrain, limited or absent mobile phones and Internet connectivity, and poor and unreliable postal services further exacerbate the situation.

The screening device that would enable same-day treatment is a high-speed, fully automated molecular assay for high-risk HPV infection, called the Xpert HPV Test. Self-sampling alleviates the need for clinical staff to screen such women directly, according to Vallely. “By readily identifying women who have a high-risk HPV infection, this clinic-based, self-sampling strategy would allow health services in low-income settings such as Papua New Guinea to focus their efforts on those women who are most at risk of cervical pre-cancer and cancer,” he says.

Once a woman is identified as being at increased risk for cervical cancer by the Xpert HPV Test, she immediately undergoes treatment, according to Vallely. In Papua New Guinea and similar settings, this treatment entails painting her cervix with vinegar, he says. Its acetic acid causes precancerous lesions, which otherwise are not visible, to stain white. Clinicians then ablate the lesions using cryotherapy—a relatively noninvasive procedure that allows such patients to return home the same day. Women who have developed outright malignancies are referred to specialists.

“If implemented properly, this advance could tremendously increase screening coverage in many regions of the world with high cervical cancer burdens,” says Patti Gravitt, of Johns Hopkins Bloomberg School of Public Health in Baltimore, Md. “Most studies showing this level of comparability at the viral detection level between self-collected and cervical samples have translated to comparable sensitivity for pre-cancer.”

Papua New Guinea has a very high burden of cervical cancer, Vallely says. The rate of new cases is six to seven times higher than in Australia and New Zealand, and mortality is around 14 times higher, making HPV-associated cancers a leading cause of premature death for this small nation.

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RESEARCH ADVANCES
Phages Form Liquid Crystals, Shaping P. aeruginosa Biofilms
Shannon Weiman

Through a novel mechanism, bacteriophage particles link with the surfaces of Pseudomonas aeruginosa cells and other nearby polymers to form tenacious biofilms, including those that form within the lungs of cystic fibrosis (CF) patients, according to Paul Bollyky of Stanford University in Stanford, Calif., who spoke during the Bay Area Microbial Pathogenesis Symposium last March in San Francisco. Bacteriophage that reproduce within P. aeruginosa are released and can assemble into liquid crystal structures that surround and protect these bacteria as part of larger biofilms, according to Bollyky, Patrick Secor, William Parks, and their collaborators. Details describing some of this research appeared November 11, 2015 in Cell Host & Microbe (doi:http://dx.doi.org/10.1016/j.chom.2015.10.013).

In viscous environments, P. aeruginosa cells upregulate their expression of filamentous phages as the cells begin to form biofilms, according to Bollyky. Within the lungs of CF patients, these long, negatively charged viruses interact with a broad variety of host and microbial polymers, including DNA molecules, mucin, and hyaluronan, forming stable liquid crystals as part of a larger and heterogeneous biofilm matrix. This structure confers multiple fitness advantages on the P. aeruginosa cells, helping to explain how biofilms enhance their pathogenic properties. “One of the canonical features of biofilms is their ability to adhere to surfaces,” says Bollyky. “Filamentous phages make structural contributions to biofilms that increase adhesion.” In addition, the phage and bacterial cell-based liquid crystal structure increases the viscosity of mucosal secretions, a hallmark symptom for CF patients. Thus, P. aeruginosa biofilms are very difficult to dislodge from the lungs of such patients, obstructing airways.

Liquid crystals also retain water, protecting P. aeruginosa cells against drying out while promoting their survival and transmission. “The transmission of P. aeruginosa from one CF patient to another can occur through aerosols or contaminated surfaces, and desiccation tolerance is thought to be critical to transmission,” says Bollyky. Indeed, highly transmissible P. aeruginosa isolates harbor filamentous prophage capable of generating such liquid crystal biofilms.

These structures also protect bacteria against some types of antibiotics by sequestering positively charged drugs such as aminoglycosides within the negatively charged matrix, helping to explain why bacterial pathogens in biofilms resist treatment with such drugs, according to Bollyky. The matrix may also protect pathogens within them against host innate immune defenses by similarly sequestering cationic antimicrobial peptides. These data suggest that filamentous phage contribute to the persistence of P. aeruginosa biofilm infections and may help explain how filamentous phage influence P. aeruginosa virulence in vivo,” he says.
He notes that particularly virulent clinical isolates, notorious for causing intractable lung infections, produce far more phage than do their less virulent counterparts.

Finding liquid crystals “in a medically relevant biofilm is pretty remarkable,” says James Wilking of Montana State University in Bozeman, a physicist who works on biofilm structure but was not involved in this work. Phages might be playing comparable roles for other clinically challenging biofilm infections involving other gram-negative bacterial pathogens, such as *Escherichia coli* or *Vibrio cholerae*, both of which also produce filamentous phage, Bollyky points out. Adds another biofilm expert, Scott Rice of Nanyang Technological University in Singapore, “There are reports that filamentous phage increase biofilm formation for plant pathogens. [The Bollyky] study is a very nice confirmation of the physical mechanism.”

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**NEW FROM ASM**

**New Route of TB Transmission Discovered**

Scientists have identified a new route of tuberculosis transmission, via the anal glands of mongoose that live in northern Botswana and southwestern Zimbabwe. The secretions are an oily substance where the hydrophobic bacterium, *Mycobacterium mungi*, resides. First author Kathleen Alexander of Virginia Tech in Blacksburg, Va., says the findings have implications for TB outbreak potential among wildlife and livestock: “We need to be aware of the diversity of ways that TB can be transmitted. Tuberculosis is a huge burden for the agriculture sector and environmental transmission between wildlife and livestock is an increasing concern.” The research team, headed by Mitchell Palmer of the National Animal Disease Center in Ames, Iowa, plans to study the genetic characteristics that grant *M. mungi* this new route of transmission.


**NEW FROM ASM**

**Arginine Disrupts Oral Biofilms and Shifts Bacterial Makeup**

Supplementation of L-arginine may increase oral health, finds a collaboration of scientists from Sichuan University in Chengdu, China, the University of Pennsylvania in Philadelphia, Pa., and Colgate-Palmolive Technology Center in Piscataway, N.J. When added to a multispecies biofilm, arginine promoted growth of the arginolytic *Streptococcus gordoni* over caries-causing *Streptococcus mutans*, and led to an increase in biofilm pH. First author Jin-zhi He and senior author Hyun Koo also reported that arginine treatment repressed *S. mutans* expression of genes associated with exopolysaccharide and bacteriocin production.


**NEW FROM ASM**

**Cystic Fibrosis Infectious Bacterium Evolves in Bursts**

Cystic fibrosis (CF) patients, as described by first author Inêz Silva in an *mSystems* report. The research team, led by Leonilde Moreira, examined a series of isolates collected from a single CF patient over 20 years. Sequence and analysis of 22 *B. multivorans* isolate genomes showed that new lineages evolved mainly by mutations in genes with regulatory or signaling roles, and in genes involved in metabolism. “This dynamic suggests that monitoring these evolutionary and molecular patterns could be used to design responsive therapies designed to limit population diversity and disease progression,” says Moreira.