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Microcosm

Fall 2019

ASM's Focus on Global Public Health

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AMERICAN SOCIETY FOR MICROBIOLOGY

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from the editor

Science is an international endeavor. We never know where the next great idea or creative method will be developed, so there is a compelling need to meet colleagues at international conferences like the ASM Microbe meeting, and to collaborate with scientists from around the world.

As highlighted in this issue of *Microcosm*, there is probably no area of microbiology that requires a more obvious need for international cooperation and collaboration than public health. Diseases are rapidly transmitted around the world, both through natural channels and on planes, ships and trains, which are constantly moving people and goods to all corners of the globe. Awareness of where and when disease outbreaks occur enables more accurate predictions of where they might go next, facilitating preventive measures. However, for these public health approaches to work, the free exchange of information between public health agencies in different countries is imperative — but this seemingly simple problem can be thwarted by political agendas. For example, news about an outbreak of influenza, Ebola or a variety of other diseases can quickly reduce tourism, providing a financial incentive to keep this information from the public. The ASM and public health agencies have worked to promote international cooperation that ensures the fast and forthright exchange of public health information, facilitating quick, coordinated responses to outbreaks of disease.

Useful exchange of information between public health agencies and the effective treatment of disease depends upon the quality and reliability of laboratory data, both in regions with advanced clinical capability and in regions with limited laboratory infrastructure. Another way that ASM contributes to global health is by helping to build capacity in clinical laboratories from resource-limited regions. Over 500 ASM members who are subject-matter experts have contributed technical assistance, training and mentoring to these projects. Their efforts focus on helping to establish sustainable, quality-assured diagnostics, quality-management systems, biosafety and biosecurity, strategic planning, outbreak detection and response and workforce development.

Many ASM members from across the globe contribute to public health, clinical microbiology and the basic research that drives important new scientific discoveries. International cooperation requires bringing together people with different experiences, backgrounds and values to achieve common goals. This diversity of knowledge, experience and perspective is crucial to promote public health and to advance science.

The distinctive perspectives of ASM members are essential for stimulating us to consider different ideas and to push science in new directions. Hence, feedback from ASM members is crucial for our society. A recent letter to the editor from Mimi Goldschmidt questioned key conclusions from a *Microcosm* article about Pat Brown and the Impossible Burger. She pointed out that questions remain about the safety of this meat substitute, noting possible concerns about the health effects of leghemoglobin. Although the *Microcosm* article was a summary of Brown's talk at the ASM Microbe 2019 meeting, not an assessment of the science behind the Impossible Burger, we appreciate these comments and encourage other readers to provide feedback as well. We are planning a new section on the ASM website that will engage member feedback and discourse.

Whether you are addressing a global health problem, interacting with colleagues from different places, or sharing ideas that stimulate thinking about problems differently, ASM is a wonderful resource for engaging with other scientists and learning new concepts.

Stanley Maloy, Ph.D.
Editor-in-Chief

15 Years of PEPFAR

Sustainable Interventions for an HIV-Free Future

by Elyse Franko-Filipasic

When the George W. Bush administration launched the President's Emergency Plan for AIDS Relief (PEPFAR) in 2003, infection by HIV was equivalent to a death sentence in much of the world. Given the lack of resources for diagnostics and treatment, many countries were faced with soaring HIV infection rates that were largely going unchecked.

By expanding access to preventive services, antiretroviral (ARV) treatment and patient care, PEPFAR has helped transform the global dialogue to combat HIV/AIDS. We now know that, with strategic investments in resources and program-implementation, the course of this deadly disease can be reversed — and, with continued action, eliminated.

When it celebrated its 15th anniversary last year, PEPFAR's total investments had surpassed more than $85 billion. This makes it the largest commitment by any one nation to address a single disease — and with an estimated 17 million lives saved in 50 countries worldwide, the plan's success is a testament to the ability of targeted, evidence-based policies to make lasting, sustainable change.

ASM has supported the U.S. Centers for Disease Control's (CDC) PEPFAR strategy as an implementing partner since 2006. Over the past 13 years, ASM has worked with teams in 19 PEPFAR focus countries to advance microbiology solutions through trainings, develop evidence-based national policies and strengthen laboratory services.

Our initiatives have helped to provide lifesaving HIV testing and diagnostic services to the underserved populations who need them most. However, as much as we love seeing our work produce meaningful results, we know that the most important aspect of any public health program is sustainability. This is why our focus has always been on capacity-building at the local level. We've worked closely with in-country teams to develop robust laboratory strategies in line with PEPFAR's four key priorities:

PROGRESS: To save lives, prevent new HIV infections and accelerate progress toward HIV/AIDS epidemic control.

POLICIES: To ensure that investments are optimally focused for impact through data-driven policies — and support partner countries in developing policies of their own.

POPULATIONS: To identify and reach the populations most affected by the HIV/AIDS epidemic, using innovative solutions to meet their needs.

PARTNERSHIPS: Leveraging cross-sector partnerships to increase impact and ensure sustainability.

Measurable Progress

PEPFAR's success is due in large part to its focus on sustained, measureable progress on expanding access to HIV diagnosis and treatment. By September 2018, it was estimated that PEPFAR had helped 95 million people get tested for HIV, provided 14.6 million people with lifesaving ARV treatment, and prevented mother-to-child transmission in 2.4 million infants. By encouraging people to know their status and seek necessary care, PEPFAR has been a driving force behind progress toward the UNAIDS 90-90-90 targets.

ASM's capacity-building programs are helping laboratorians build the skills they need to provide lifesaving testing services, establish internationally recognized standards of practice, and pass on their expertise to future generations. In addition to expanding access to HIV testing, ASM has worked to strengthen diagnostics for tuberculosis (TB) and other opportunistic infections that present heightened risks for HIV-infected patients.

Our successes have taken many forms. In Botswana, ASM delivered trainings and supported the development of a combination prevention and treatment package as part of the four-year Botswana Combination Prevention Project (BCPP). The BCPP helped Botswana reach its UNAIDS 90-90-90 targets before the 2020 deadline, with more than 95% of those on treatment estimated to have reduced viral loads in 2019.

In Mozambique, which has one of the highest rates of HIV-TB co-infection worldwide, ASM partnered with local laboratories to implement step-down training initiatives on biosafety and drug-susceptibility testing. And in Zambia, ASM joined the University Teaching Hospital TB Laboratory in Lusaka on its eight-year journey toward international accreditation: Through the continued improvement of its quality-management system, the laboratory received its ISO 15189 accreditation — the first awarded in the country — in November 2018.

Data-driven Policies

Effective public health spending can only be achieved with meaningful, data-driven policies. In PEPFAR countries, this often means building robust data-gathering and -monitoring practices from the ground up. In 2018, ASM rolled out a pilot platform for tracking viral load test results in the Democratic Republic of the Congo (DRC). Once the platform expands to facilities throughout the country, it will help policymakers track testing data at the national level — and ensure that HIV-infected patients in DRC are receiving the treatment they need to suppress their viral loads in line with UNAIDS targets.

Working with extensive in-country partner networks, ASM has also developed policies to bolster biosafety and surveillance systems. In Tanzania, ASM helped draft a national surveillance framework to help combat antimicrobial resistance (AMR) — an issue particularly relevant to PEPFAR's work due to the comorbidities between HIV and drug-resistant TB infections. ASM also helped to draft a similar AMR surveillance plan in Ethiopia and to establish a framework for laboratory biosafety in Mozambique.

PEPFAR program participants in Tanzania and Mozambique.

Populations

Sustained progress on meeting targets for HIV diagnosis and treatment is dependent on reaching the world's most vulnerable populations. While we have a good idea of what needs to be done in the countries with the highest HIV/AIDS burdens, there are many barriers to putting those strategies into practice. Often, these take the form of infrastructural bottlenecks that disrupt laboratory sample transport and prevent patients from getting tested and diagnosed.

In Côte d'Ivoire, for example, access to testing

PEPFAR Countries

services has traditionally been quite limited. Until recently, many remote areas had no laboratory services at all. Patients had to make an expensive, full-day journey to the capital, Abidjan, to be tested for HIV infection. ASM has been working to bring laboratory services to these underserved areas with the establishment of local testing sites and modular molecular laboratories (MMLs) — containerized laboratories that can be constructed and transported at low cost.

Meite Syndou
ASM Young Ambassador

"As the head of the first ASM container laboratory in Côte d'Ivoire, at the Yopougon University Hospital Center, I was able to observe ASM's commitment to the fight against infectious diseases — and especially HIV. From 2015 to 2019, our laboratory conducted approximately 50,000 viral load tests and 3,000 early-infant diagnostic tests. The success of this project resulted in the opening of several other container laboratories across the country."

Between 2016 and 2019, ASM opened eight MMLs and 38 pre-analytic testing sites throughout the country, with the goal of expanding access to early-infant diagnosis of HIV infection and viral load testing. The addition of these new facilities helped expand testing coverage in Côte d'Ivoire from 10% to 62% in just two years.

Partnering for Greater Impact

Our successes would have been impossible to achieve without the help of partners around the world. Collaborations with other implementers, country governments, medical universities, local microbiology experts and national and local laboratories have ensured that our efforts and funding go where they are needed most.

ASM's partnership with the CDC has been a cornerstone of all our PEPFAR-related work. We've worked with CDC offices in the U.S. and abroad to develop capacity-building trainings and workshops for HIV and TB testing, to expand access to testing services, and to help laboratories set standards for quality practices and biosafety.

For the past eight years, this partnership has also helped us train and facilitate knowledge exchange among laboratorians from six low- and middle-income countries with the CDC-ASM Fellowship Program. With a core curriculum based on a quality-management-systems approach, the three-week Fellowship Program takes place each summer at the Indiana State Department of Health laboratory. Fellows have gone on to implement new standards for quality assessments and quality assurance in their home countries, both at their local institutions and at the national laboratory network level.

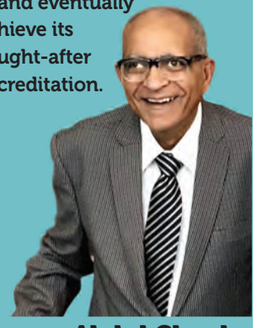
Moving forward, fostering our network of dedicated partners will continue to be key — not only for implementing our programs, but also for ensuring that they can be maintained and scaled for lasting impact. While funding mechanisms and government priorities can change, encouraging knowledge-sharing and local capacity-building will ensure that lifesaving diagnosis and treatment for HIV/AIDS are available for all who need them.

Elyse Franko-Filipasic is a writer and communications specialist focusing on global health and health policy. Since 2016, she has been the lead editor for ASM's *Global Impact Report*. Elyse is based in Berlin and holds a M.Sc. in International Public Policy from University College London.

'What are your needs — and how can we help you?'

This was the key question that led to success in achieving the first ISO 15189 laboratory accreditation in Zambia, according to ASM Consultant Abdul Chagla. While international implementers might establish their own agendas and standards for success, sustainable impact can only be achieved with local input.

So when local laboratorians at the University Teaching Hospital TB Lab in Lusaka spoke, we listened. At their request, Chagla and other ASM consultants helped establish standards for proper documentation and held capacity-building workshops for lab managers. These helped the laboratory move from one star to five stars on the Stepwise Laboratory Improvement Process Towards Accreditation (SLIPTA) checklist — and eventually achieve its sought-after accreditation.



Abdul Chagla
ASM Consultant

George F. Gao walks briskly through the George R. Moscone Convention Center in San Francisco, where he's just taken part in an animated panel discussion about the contributions of microbiologists in the international response to outbreaks like Ebola.

George F. Gao

Learning on the Ground and on Your Feet

by Julie Wolf, Ph.D.

Five years ago, Gao was in a much different setting. The West African Ebola outbreak had been ongoing for several months and showed no sign of containment. As then-Deputy Director-General of China Centers for Disease Control and Prevention, Gao spent two months in West Africa with his China CDC team as they assessed the on-the-ground infrastructure and opened mobile testing labs for diagnosing infected patients.

The Ebola outbreak began in Guinea, and fear of the spreading infection led Guinea to close its borders with Sierra Leone and Liberia to contain the disease.[1] The number of reported cases continued to grow through the end of 2014, peaking in September in Liberia and in November in Sierra Leone. The motivation to contain an outbreak is understandable, but man-made borders aren't respected by infectious disease. "Any pathogen, any virus — they don't need a passport to travel," Gao says. "They don't need a visa."

Unlike microorganisms, Gao does need a passport, and his is well-worn. "Two days ago, I was in Sydney," he says. "Today, I'm sitting in San Francisco. In two days, I'll be in Beijing." Gao's intense energy belies any exhaustion he may be feeling due to his rigorous schedule. His roles as director-general of the China CDC, as professor and director of the Chinese Academy of Sciences Key Laboratory of Pathogenic Microbiology and Immunology and as vice president of the National Science Foundation of China make Gao an in-demand scientist around the world. His expertise has helped in the fight against SARS, Ebola and Influenza, among other infectious diseases.

Gao is sitting on the panel because of his experience on the ground during outbreaks, but his basic scientific training has clearly influenced his ideas about public health applications.

Over the course of the next hour, two experiences echo repeatedly throughout our conversation: one, field work is vital for scientists to understand the real-world applications of their scientific discoveries, and two, basic science is fundamental for laying a foundation upon which new scientific applications can be built.

Coordinating China's Role in the Ebola Response

Gao and China CDC played a critical role during the 2014-16 Ebola outbreak in

"Microbiology Researchers at the Front Lines of Infection Outbreaks" session at ASM Microbe 2019. (Left to right) Christopher W. Woods, Mark Lim, Jennifer Gardy, Christian Happi, George F. Gao and Scott Teesdale.

West Africa, building the infrastructure necessary for patient testing, treatment and recovery. Gao had pushed for these actions after spending time in Sierra Leone, arguably the heart of this outbreak. His visit informed the China CDC response as the case numbers continued to build throughout Guinea, Liberia and other West African countries.

The epidemic began in late 2013 in a small village in Guinea, likely due to a spillover event from bats. It was officially declared an epidemic by the World Health Organization (WHO) in March 2014, and by July of that year the outbreak had spread to the capitals of neighboring Liberia and Sierra Leone. This was the first urban Ebola outbreak where the larger, denser population meant person-to-person transmission occurred more easily and became harder to trace. It was Gao's experience in Freetown, Sierra Leone, that spurred him to pen a column in *Science* about daily life amid a growing outbreak.[2]

Gao visited Sierra Leone in 2014. While there, he recognized the role that infrastructure plays in both spreading the disease and putting a stop to its transmission. At that time, Sierra Leone had fewer than 100 registered doctors to identify sick patients, as well as scarce facilities to properly quarantine, treat and rehabilitate the infected. Gao recognized that not only would better infrastructure be necessary to quell the epidemic, but also more boots on the ground.

China provided not only badly needed infrastructure and supplies during the epidemic, but also hundreds of trained medical workers who worked in concert with U.S. and West African workers. China was also the first to set up a medical facility in Liberia, providing 280 medical staff.[3] The workforce and infrastructure China provided, such as mobile Biological Safety Level 3 (BSL3) laboratories to safely test and diagnose patients, was critical to successfully quenching the outbreak, which was officially declared over in June 2015, two-and-a-half years after the index case.[4]

On-the-Ground Development of Basic Technologies

Gao's on-the-ground experience helped him gauge the real-time environment in Africa. Back in San Francisco, he explains how all scientists should spend time away from the bench to better understand the everyday challenges in disease-endemic regions. "Everyone should go [to these regions], including those who are doing basic research, like me," he says. "What is the most important scientific question to be answered? You can only learn this by going into the field." Traveling to the field is especially important for those who work in medically related or public health fields. "That tells you where the problem is, what the major issues are and what the hurdles are for implementation of public health measures," Gao says.

> "Traveling to the field is especially important for those who work in medically related or public health fields. That tells you where the problem is, what the major issues are and what the hurdles are for implementation of public-health measures."

Gao's true passion is basic research. He trained as a veterinarian in China immediately after China's cultural revolution, then earned his doctorate from Oxford and did a postdoctoral fellowship at Oxford and Harvard to specialize in structural biology. His lab has characterized structures of viral, bacterial and host proteins important for infection, and his affection for these fundamental discoveries may be why he sees basic research as foundational for applied and public health microbiology.

Take nucleotide sequencing, for example. "Some would say [sequencing] looks like basic research, that A, G, C, T nucleotide sequence has nothing to do with public health," Gao says. "But that's wrong." Sequencing plays many roles during an outbreak, including providing an answer to the following question: Would vaccine research-development efforts be in vain?

In Freetown and other urban centers, the Ebola virus was passing from person to person in long chains of transmission that had not previously occurred. As a virus enters a new host species (in this case, human beings), it needs to adapt. "We ran quite a few virus sequences, which told us that the virus mutates very quickly," Gao says. Such rapid viral adaptation may influence the immune response to the virus or, worse for vaccine development, key viral protein epitopes. Gao's team generated 175 genomes by whole-genome sequencing, allowing statistical scrutiny of the phylogenetic analysis.[5] The scientific team used this technology to confirm that the virus' mutation rate would likely not affect the efficacy of vaccines then under development (and since produced) based on historically isolated viral strains.

The Ebola outbreak facilitated the on-the-ground application of still-developing technologies, including new sequencing technologies. At the onset of the West African Ebola epidemic, the pocket-sized Nanopore DNA sequencer was still new to the sequencing world and not yet commercially available. Its accuracy was also of concern, and proof-of-concept trials had been largely run in controlled lab settings.[6] However, its portability and quick data turnaround allowed scientists to quickly assess and halt the chains of disease transmission, proving that basic research to develop methods can have important public health utility[7] — including new methods addressing what might be considered "solved" problems.

Basic Research Lays the Foundation for Public Health

In addition to the development of new methods and technologies, Gao encourages a very basic application of these sequencing technologies: descriptive science. One of Gao's recent collaborative projects is the Global Virome Project, which aims to detect the majority of the planet's unknown viral pandemic threats. The ambitious goal is to prepare for future pandemics so that public health officials can take a proactive, rather than reactive, stand against disease outbreaks.

The Global Virome Project was announced with great fanfare among the disease ecology and biopreparedness communities, but not without skepticism about the useful application of the collected data.[8] Gao supports the Global Virome Project, citing his experiences with SARS, MERS and Ebola as viruses that emerged to cause major outbreaks, and was one of the authors of the *Science* announcement.[9] However, he remains practical about the finances involved. "The potential to have an emerging virus is always there, so of course I think it's worthwhile," he says.

Merely listing the global population of viruses won't suffice for pandemic preparedness, since determining the risk from each new virus requires careful study. How can scientists understand which viral characteristics they should assess to prevent the next outbreak? Gao's answer: basic science, such as what he does in his own lab. "My work is on interspecies transmission," Gao says. "Through adaptation, through evolution, some viruses may adapt to human beings." These adaptations, Gao says, can be detected through the basic research that might help to define characteristics of zoonotic viruses or the receptors likely to interact with human ligands. Answering the why and how surrounding these characteristics, what one might call "mechanistic studies," can help to determine which viruses should be monitored for potential human transmission.

Much of Gao's research efforts come from his role with the Chinese Academy of Sciences, where he runs a lab of around 20 scientists. Gao has amassed a collection of sera from many different sources: various species, geographies and time points. He shares these through collaborations with disease researchers who want to study their favorite microbe. This generosity of collaboration is one reason why Gao has published on Ebola virus, Rift Valley Fever virus, Chikungunya virus, enterovirus B, human immunodeficiency virus, hepatitis C virus, tick-borne encephalitis virus and yellow fever virus — all in 2019

> "My work is on interspecies transmission. Through adaptation, through evolution, some viruses may adapt to human beings."

(plus work on ribosome biogenesis, bat immunity and PD-1 tumor immune checkpoint therapy).

Gao sees collaboration for projects like the Global Virome Project as vital to the scientific process. However, collaboration alone is not the road to a successful scientific career. "To promote the science, to promote public health, to promote societal development, we need 4 Cs, which are collaboration, communication, coordination and competition," Gao says. "Don't forget: Competition is very important." Gao believes that scientists who leave the comfort of their labs benefit from speaking with their colleagues about the important questions in other lab settings and disciplines. Interdisciplinary communication is where new ideas are hatched, he explains, and often relationships between scientists contain parts from each "C" category.

Gao's newest role, as vice president of the National Science Foundation of China, gives him the opportunity to promote interdisciplinary cross-pollination. He allocates funds for life sciences and medical sciences in this role, putting him in a position to decide whether to fund the basic research that he clearly values, or the development of applications derived from some of these basic discoveries, which are often more highly valued by the public. A balance between basic and translational research can be difficult to achieve.

"In the whole world, from the U.K. to the U.S. to China, we haven't solved that problem," he says. "Sometimes, it's very hard to identify which basic research has potential for translation. Of course, we are trying very hard to identify some potential basic research to put into translational application." Gao speaks admirably of the U.S. system, which not only offers government funds through NIH- and NSF-funded grants for academics and small businesses, but also has a well-connected venture-capitalist network to provide private funds. These networks can help identify and support scientists who want to develop their discoveries into innovative products for the commercial market.

There Is Only One Subject: The Earth

Getting out of the lab and into real-world situations where scientists must interact with society and other researchers can help answer questions that require multiple scientific disciplines. "We don't have subjects divided by nature," Gao says. "We ourselves, because of the limitation of our knowledge, limitation of our mind, limitation of our memory, we human beings divide it into different subjects. But when you go out to the field and look at nature, there's only one subject, and that's the Earth." Preparing oneself with interdisciplinary studies, such as Gao's background in veterinary medicine, structural biology and protein chemistry, can prepare a scientist to address truly interdisciplinary questions. Gao considers himself a student of all of nature, proclaiming, "I am a biologist."

Gao clearly has many roles to fill, including guiding the China CDC efforts in the current Ebola outbreak in central Africa.[10] Despite his many duties, when Gao dedicates his attention, his focused and thoughtful answers reveal a quick, ever-processing mind. In thinking about the many roles in basic science and public health that Gao must juggle, one might wonder whether Gao carries a recently discovered mutation that allows some people to survive and thrive on four hours of sleep.[11] Gao laughs at the suggestion: "I get seven or eight hours; I'm a normal person!" After a brief pause (Gao only ever pauses briefly), he continues, "What's important is how you spend your time awake."

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Young Women Explore Microbiology at WiSci Estonia

by Alexis Rose

Across the globe, women are systematically underrepresented in science, technology, engineering, arts and design and mathematics (STEAM) careers. For example, only 28% of the world's researchers are women, and from 1903-2017, only 17 women (versus 572 men) received Nobel Prizes in physics, chemistry and medicine.

These gender disparities are an unfortunate reality today, but the Women in Science (WiSci) Girls' STEAM camp aims to change that fact.

WiSci Girls STEAM Camp | Estonia

WiSci, a two-week-long, all-expenses-paid camp for young women, brings together female-identifying secondary school students from around the world to learn from scientists at ASM, Google, NASA, Intel and more. One of this year's WiSci camps took place in Tallinn, Estonia, and I had the opportunity to co-facilitate a microbiology-focused workshop with 100 students from Eastern Europe and the U.S. Together with ASM Young Ambassador Dr. Triinu Visnapuu (see her profile on page 32 of this issue), we explored the invisible world of organisms that live in us, on us and around us through hands-on educational activities.

In one activity, the students assembled an innovative and affordable scientific tool: the Foldscope. This portable paper microscope is built in less than an hour and magnifies samples up to 140x. Dr. Visnapuu and I gathered specimens ahead of time, using easily accessible items such as onion skin, pond water, lettuce and yeast. Then, during class, the girls used tweezers and scissors to cut tiny samples to mount on slides.

After the Foldscopes were assembled, one curious student went hunting for more samples in the hallway and spotted a bug. She collected it, then mounted it on a slide to examine its microscopic parts. ASM provided each student with a Foldscope to take home, so they could continue their scientific inquiry in their own communities and

Dr. Triinu Visnapuu, ASM Young Ambassador, greets students before the microbiology workshop at WiSci Estonia.

Students try their hand at creating agar art using naturally colorful bacteria.

A student peers through the lens of her Foldscope, a portable paper microscope capable of 140x magnification.

More than 50 STEAM Students participated at WiSci Estonia.

Photos by Alexis Rose

be inspired to pursue the microbial sciences for life.

In another activity, Dr. Visnapuu showed the students how to create agar art using petri dishes as canvases and naturally colorful bacteria (such as *Serratia marcescens* and *Bacillus mycoides*) as paint. It was incredible to see this blending of art and science, and it was clear that the students really enjoyed themselves.

After the ASM workshop, the students shared overwhelmingly positive feedback, saying things like:

- **"Microbiology is a cool, interesting STEAM field."**
- **"I learned that I really enjoy microbiology!"**
- **"Microbiology is a fun thing ☺"**

Science is an important component of girls' education at every age, but it is imperative that STEAM training is a major focus at the middle and high school levels in order to put girls on a science trajectory. Workshops like WiSci aim to engage girls at a critical time period when they are forming opinions about their abilities and making decisions about their futures. By enhancing girls' STEAM skills through hands-on experimentation, we can inspire young women to become leaders in science.

To learn more about WiSci and its mission, please visit www.girlup.org/wisci.

To become involved in ASM's Global Public Health Programs as a consultant, volunteer or country ambassador, please visit **www.asm.org/globalhealth**

Imagine a world where antibiotics don't work. Where a bout of food poisoning, a cut from working in the yard or a simple bladder infection becomes a matter of life or death. This grim reality is rapidly approaching and, in some cases, has arrived.

Antimicrobial Resistance Keeps Me Up At Night

by Robin Patel, ASM President

This was not the case when I graduated from medical school. From the 1940s through the 1980s, we had reliably effective antibiotics. During my training, advising on how to treat critically ill, septic patients seemed simple. When paged in the middle of the night, I felt so comfortable with the medical advice I was dispensing that I could hang up the phone and fall right to back to sleep.

> ***Medical experts can no longer count on available antibiotics to work in every case, and it's getting worse year by year.***

Today, though, antimicrobial resistance (AMR) keeps me up at night. Medical experts can no longer count on available antibiotics to work in every case, and it's getting worse year by year. A 2019 report by the World Health Organization predicts that drug-resistant infections may become the leading cause of death, claiming up to 10 million lives annually (surpassing cancer deaths), by the year 2050 if AMR is left unchecked.

As a clinical microbiologist and infectious diseases physician, I work with bacteria every day. Bacteria exposed to an antibiotic in the lab readily develop resistance to that antibiotic, by mutating their own genes or acquiring genes from other bacteria — something they are naturally equipped to do. Unfortunately, once bacteria become resistant to an antibiotic, they do not necessarily revert to being susceptible to it when the antibiotic is no longer around. Humans have taken antibiotics for granted; antibiotics have cured infections that previously killed patients and have enabled us to perform complicated surgeries and transplants and cure cancer. But now, because of AMR, we can't always count on them to work — and we can't turn the clock back to completely rid the world of resistant bacteria.

So, what can we do? We need to improve how antibiotics are used in humans and animals by restricting their use to situations where they are needed. We need new antibiotics, and we need to reserve newer antibiotics only for appropriate situations, setting the stage for slower evolution. We need research to better understand mechanisms of resistance and how we can avoid selecting for resistance, as well as how our interactions with each other, animals and the environment impact the spread of resistant bacteria. We need innovative, rapid diagnostics that quickly identify whether patients need antibiotics, because, in addition to the potential for selecting for resistance, there are other potential harms to taking antibiotics unnecessarily. Resistant bacteria that emerge in one geographic locale often spread globally, and at an amazingly fast pace.

ASM is playing its part in this global fight. Our international members and public health teams are on the ground in communities, empowering local microbiologists through training and long-term mentorship aimed at guaranteeing sustained quality microbiology laboratory practices.

Today, some rapid diagnostics capable of identifying bacteria and their resistance factors are available or within reach. Tracking changes in microbial populations (AMR surveillance) is helping detect resistant bacteria and allowing quick action around potential outbreaks across communities. These surveillance findings are crucial to informing clinical therapy decisions and guiding policy recommendations.

While I note the progress in combatting AMR, I acknowledge the long road ahead of us. There are numerous barriers to progress; it is crucial that global stakeholders work together to achieve solutions. And those global stakeholders are us — all of us.

Help ASM Promote Diversity and Inclusion in the Microbial Sciences

To address the gap in diversity and inclusion, ASM will launch an ASM Diversity, Equity and Inclusion project (DEI), a yearlong study that aims to make the microbial sciences more inclusive.

In the last three decades, ASM has supported 650 minority fellowships, travel grantees and honorific awardees. In 2000, former U.S. President Clinton honored ASM with the Presidential Award for Mentoring Underrepresented Minorities in Science and Engineering due to its leadership role in supporting minority fellows. In 2000, the NIH named ASM a sole partner in sponsorship of the largest undergraduate minority student STEM conference: the Annual Biomedical Research Conference for Minority Students (ABRCMS).

Despite substantial efforts to recruit and recognize underrepresented minorities in the microbial sciences, there is scant diversity among ASM editorial boards and reviewers, scientific and clinical achievement awardees, conference speakers and in our governance. To address these concerns, the ASM Board of Directors (BoD) convened an external task force to conduct a review of practices in the microbial sciences. This task force will be responsible for identifying a plan to holistically integrate diversity into ASM and ensure inclusive standards of practice across the discipline.

The task force will serve for one year as an external, advisory group for the BoD. A significant and critical component of the project is member engagement. Members will be called for feedback through discussions, interviews, surveys and social media, and this data will inform ASM's next strategic steps.

To get involved or share feedback, please fill out this survey:

www.surveymonkey.com/r/asmdei

ASM's Global Public Health Programs Partnership with IRESSEF and NIH Pakistan

ASM's Global Public Health Program is collaborating with an international network of microbiology experts to ensure that public health systems around the globe can improve the health and well-being of their populations. In some instances, ASM deploys microbiologists to provide training, mentorships and direct technical assistance to strengthen a country's clinical and veterinary laboratory services. All of these efforts aim to supplement, strengthen and sustain local microbiology capacity through long-term collaborations with local microbiologists and institutions. This is a core value for ASM as a society that advances the microbial sciences.

Among ASM's many partner institutions, Senegal-based Institut de Recherche en Santé, de Surveillance Epidémiologique et de Formation — Institute for Health Research, Epidemiological Surveillance and Training (IRESSEF) and the National Institutes of Health (NIH) Pakistan are two training institutions for laboratory-strengthening programs that exemplify complementary expertise in microbiology. Senegal-based IRESSEF, a subdivision of the microbiology and virology division of the Université Cheikh Anta Diop, has quickly become a hub for health research, surveillance and training for the African continent. NIH Pakistan is a research and training institution that plays a significant public health leadership role for the country.

ASM staff with IRESSEF team visiting Sengal's public health laboratory in Thies.

IRESSEF

IRESSEF is located in Diamniado, a newly-built city in the suburbs of Dakar. Thanks to support from the Government of Senegal and the GILEAD Foundation, IRESSEF launched under the direction of Prof. Souleymane Mboup. With a dynamic multidisciplinary team, scientific leadership provided by Senegalese and foreign academics, and state-of-the-art laboratories holding ISO 15189 and 15190 accreditations, IRESSEF offers a unique working environment in the West African subregion.

Currently, IRESSEF provides several platforms, including modern molecular biology, immunology, virology, bacteriology, biochemistry and hematology laboratories and level-three biosafety laboratories. Through IRESSEF, scientists have access to a well-equipped biobank, a medical analyses laboratory, maintenance and metrology units, a clinical trials department, a health and demographic surveillance system covering a population of 30,000, a clinical trial center and a modern training center.

The vision for IRESSEF is to serve as a hub of excellence in research and training on tropical infectious diseases through expertise and technical platforms comparable to those of research institutes in developed countries. To achieve this vision, IRESSEF has a five-year strategic plan articulated around two main objectives: (1) carrying out research programs in accordance with the highest ethical and deontological standards; and (2) training an elite corps of Senegalese and African scientists who are internationally competitive and capable of fostering health research in Africa. The role of international partners is paramount to accomplishing these goals.

NIH Pakistan

NIH serves as the National Public Health Institute of Pakistan under the Ministry of Health. Established in 1967, the institute provides public health services across Pakistan and continues to make developments in laboratory sciences, vaccine and antisera production, food and drug quality testing, research and development, and capacity-building. NIH Pakistan coordinates with provincial and health development partners domestically and internationally for state-related public health functions.

NIH Pakistan has strengthened its outbreak detection and response capabilities, as well as its coordination with WHO. NIH is also strengthening its disease surveillance and response through integrated disease surveillance and response system implementation, coordination and linkages, particularly PHE. NIH Pakistan collects national data on epidemic-prone diseases and accordingly issues guidelines, alerts and advisories.

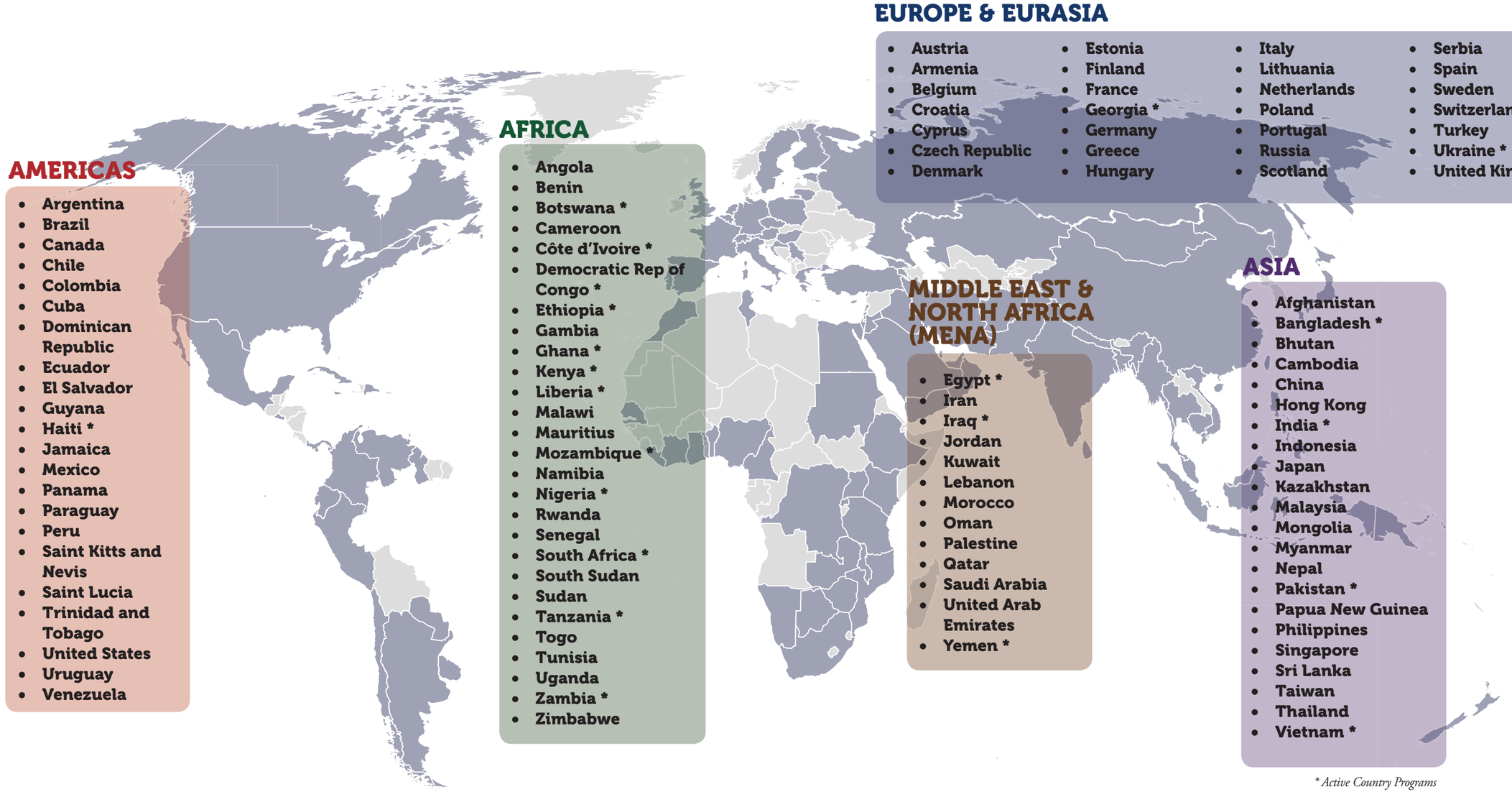
The public health laboratories division serves as the national referral center for epidemic-prone, emerging and re-emerging diseases. NIH Pakistan is now a major hub for capacity-building on traditional and advanced diagnostics, emerging cross-cutting concepts like bio-risk management, and laboratory quality-management systems. The institute also hosts field epidemiology and laboratory training programs. Recently, there has been remarkable enhancement in operational and transitional research, as well as in collaborative activities with internationally well-reputed institutes and organizations such as National Academies of Sciences, Engineering and Medicine (NASEM), National Institutes of Health (NIH), American Society for Microbiology, Bill & Melinda Gates Foundation and United States Pharmacopeia (USP). The institute is aiming to enhance its capabilities to support national public health agendas, achieve global health security and increase its public health impact.

Where We Are

Our mission is to translate microbiology expertise and tools into sustainable global public health solutions. Currently, ASM has a presence in 112 countries; that includes our active laboratory capacity-building programs. We center our approach on workforce development, biorisk management and disease surveillance.

22 Active Country Programs*

95 Country Ambassadors
83 International Young Ambassadors
34 U.S. Young Ambassadors



AMERICAS

- Argentina
- Brazil
- Canada
- Chile
- Colombia
- Cuba
- Dominican Republic
- Ecuador
- El Salvador
- Guyana
- Haiti *
- Jamaica
- Mexico
- Panama
- Paraguay
- Peru
- Saint Kitts and Nevis
- Saint Lucia
- Trinidad and Tobago
- United States
- Uruguay
- Venezuela

AFRICA

- Angola
- Benin
- Botswana *
- Cameroon
- Côte d'Ivoire *
- Democratic Rep of Congo *
- Ethiopia *
- Gambia
- Ghana *
- Kenya *
- Liberia *
- Malawi
- Mauritius
- Mozambique *
- Namibia
- Nigeria *
- Rwanda
- Senegal
- South Africa *
- South Sudan
- Sudan
- Tanzania *
- Togo
- Tunisia
- Uganda
- Zambia *
- Zimbabwe

EUROPE & EURASIA

- Austria
- Armenia
- Belgium
- Croatia
- Cyprus
- Czech Republic
- Denmark
- Estonia
- Finland
- France
- Georgia *
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- Greece
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- Italy
- Lithuania
- Netherlands
- Poland
- Portugal
- Russia
- Scotland
- Serbia
- Spain
- Sweden
- Switzerland
- Turkey
- Ukraine *
- United Kingdom

MIDDLE EAST & NORTH AFRICA (MENA)

- Egypt *
- Iran
- Iraq *
- Jordan
- Kuwait
- Lebanon
- Morocco
- Oman
- Palestine
- Qatar
- Saudi Arabia
- United Arab Emirates
- Yemen *

ASIA

- Afghanistan
- Bangladesh *
- Bhutan
- Cambodia
- China
- Hong Kong
- India *
- Indonesia
- Japan
- Kazakhstan
- Malaysia
- Mongolia
- Myanmar
- Nepal
- Pakistan *
- Papua New Guinea
- Philippines
- Singapore
- Sri Lanka
- Taiwan
- Thailand
- Vietnam *

** Active Country Programs*

ASM Joins Forces with Tanzania to Combat Antimicrobial Resistance in Partnership with the Fleming Fund

ASM has always taken a collaborative approach with country partners, prioritizing country ownership and local capacity-building. This is accomplished by establishing cadres of local trainers and mentors, empowering local organizations and technical experts, bolstering in-country scientific education, and promoting regional mechanisms for collaboration, knowledge transfer and experience sharing.

Most recently, ASM has collaborated with the Fleming Fund, leading a One Health-focused partnership with the Southern Africa Centre for Infectious Disease Surveillance (SACIDS) and Africare. This consortium aims to strengthen Tanzania's national antimicrobial resistance (AMR) surveillance strategy by addressing the gaps in AMR data and strengthening antimicrobial stewardship. A robust surveillance system is critical for informing patient and animal care, guiding policy recommendations and measuring the impact of health interventions.

ASM staff with two ASM microbiology experts who are supporting the implementation of Tanzania's AMR strategy. (Left to right: Koss Mensah, Professor Mtebe Majigo, Dr. Viola Paul Msangi, Mark Lim).

Photo courtesy Mark Lim

"Our ultimate goal is for Tanzania to not only have a solid base of local expertise, but also the independent capacity to control AMR through a coordinated response."
– Stefano Bertuzzi

"Our ultimate goal is for Tanzania to not only have a solid base of local expertise, but also the independent capacity to control AMR through a coordinated response," said Stefano Bertuzzi, CEO of ASM. "This requires working with Tanzanian stakeholders to strengthen national stewardship among the numerous sectors, including human, animal, agriculture, finance and environment. ASM is building upon its previous work in Tanzania and AMR, in addition to the expertise from the microbial sciences communities, to ensure that the work accomplished will be sustained," he added.

Previously, ASM worked in Tanzania during a cholera outbreak to help Tanzanians access quick and accurate diagnostics in the areas with the highest disease burden. By training 16 local mentors, who worked with regional laboratories to improve their microbiology skills, ASM helped improve laboratory capacity across all regions of Tanzania to support data-based decision-making for positive health outcomes.

A laboratory mentor in Mpanda, Tanzania working closely with the lead medical officer on microbiology capacity-building activities.

One Health is an approach that recognizes the interconnection between people, animals, plants and our shared environment in detecting and treating diseases that threaten public health. This integrated approach is important for:

- tracking changes in microbial populations that cause or exacerbate disease; and
- providing data that can be used by country programs to rapidly contain potential outbreaks through the early detection of drug-resistant strains.

Funding for this 18-month program is provided by the U.K. Department of Health & Social Care's (DHSC) Fleming Fund, a U.K. aid program that supports low- and middle-income countries in developing AMR surveillance systems, with a direct focus on laboratory surveillance.

The ASM-led consortium addresses critical gaps in AMR surveillance in humans, food and animals by:

- training microbiologists to conduct required AMR surveillance testing;
- improving access to laboratory supplies across the country;
- strengthening antimicrobial stewardship;
- developing One Health structures and fostering interdisciplinary collaboration;
- standardizing quality assurance in laboratory testing;
- promoting knowledge and understanding of appropriate use of antimicrobial drugs; and
- increasing the number of health facilities that routinely undertake bacterial culture and complete-route antimicrobial drug-susceptibility tests.

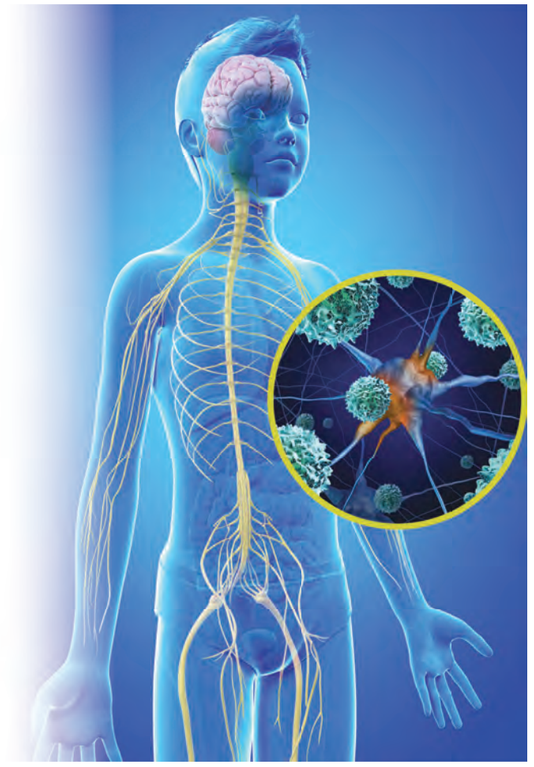
The consortium implements a train-the-trainer approach with Tanzania-based microbiologists, ensuring that veterinary laboratories have access to a cadre of expert trainers who can further train and mentor a laboratory workforce beyond the period of the project. In addition to training, the consortium ensures that laboratories have the capability to maintain essential equipment and supplies.

What's Hot in the Microbial Sciences

by Julie Wolf, Ph.D., and Stanley Maloy, Ph.D.

Scientists Hunt for Cause of Acute Flaccid Myelitis

Scientists are closing in on the cause of acute flaccid myelitis (AFM). This mysterious paralytic condition leads to loss of limb control, mostly among young children, and outbreaks of AFM have occurred every other year in the U.S. since 2014. The largest systematic study of AFM patients, published in *Pediatrics*, demonstrated one reason why a cause is hard to pinpoint: The sterile sites sampled from patients rarely contain detectable microorganisms, with oxsackievirus A16 detected in one cerebrospinal fluid (CSF) sample and enterovirus D68 detected in the serum of another among 152 sterile-site (sera and CSF) specimens. However, enterovirus, most frequently enterovirus D68, or rhinovirus was detected in 28% of 167 nonsterile-site (respiratory and stool) specimens. An *mBio* serostudy demonstrated that the CSF of AFM patients contains antibodies to enterovirus peptides at higher levels than a non-AFM cohort, lending further support to a link between enterovirus infection and AFM. Both studies concluded that although enterovirus D68 remains a top-candidate etiology, additional research is necessary.



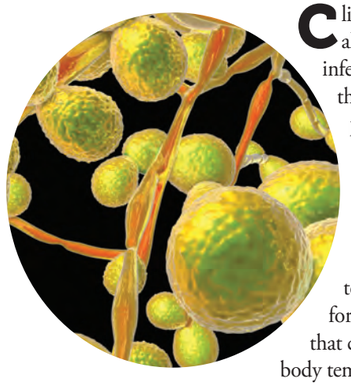
- *Ayers T.*, et al. *Acute Flaccid Myelitis in the United States: 2015-2017.* Pediatrics. *Oct. 7, 2019. https://pediatrics.aappublications.org/content/early/2019/10/03/peds.2019-1619.*
- *Mishra N.*, et al. *Antibodies to Enteroviruses in Cerebrospinal Fluid of Patients with Acute Flaccid Myelitis.* mBio. *Aug. 13, 2019. https://mbio.asm.org/content/10/4/e01903-19.*

Drug-Resistant Malaria Spreads in Asia

There is bad news on several malaria fronts: Drug-resistant *Plasmodium* is spreading in southeast Asia, and the mosquitoes that spread malaria are traveling further distances than previously thought. In two studies from *Lancet Infectious Diseases*, scientists demonstrate that *Plasmodium* resistance is rising quickly to first-line, two-drug artemisinin-based combination therapies (ACT), which are often composed of dihydroartemisinin-piperaquine. The first study, a randomized trial of the efficacy of a triple ACT, demonstrated that the two-drug combination therapy administered to a control cohort failed in 50% of patients. The second study, an epidemiological survey of *P. falciparum*, demonstrated that the co-lineage causing treatment failure had diversified into multiple subgroups and acquired new genetic features, including some associated with additional resistance phenotypes. These grave discoveries are compounded by the finding that some species of Anopheles mosquito travel via long-distance migration, published in *Nature*. An aerial sampling of mosquitoes demonstrated that the primary malaria vector, *Anopheles coluzzii,* was among the species able to travel up to 300 kilometers overnight; among the mosquitoes sampled, 80% were female, and 90% of those had taken a blood meal before their migration. These studies illustrate the seriousness of eliminating resistant *Plasmodium* parasites, as well as the challenges that will make it difficult to do so.

- *Hamilton W.L.*, et al. *Evolution and Expansion of Multidrug-Resistant Malaria in Southeast Asia: A Genomic Epidemiology Study.* Lancet Infectious Diseases. *July 22, 2019. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(19)30392-5/fulltext.*
- *Van der Pluijm R.W.*, et al. *Determinants of Dihydroartemisinin-Piperaquine Treatment Failure in* Plasmodium falciparum *Malara in Cambodia, Thailand, and Vietnam: A Prospective Clinical, Pharmacological, and Genetic Study.* Lancet Infectious Diseases. *July 22, 2019. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(19)30391-3/fulltext.*
- *Huestis D.L.*, et al. *Windborne Long-Distance Migration of Malaria Mosquitoes in the Sahel.* Nature. *Oct. 2, 2019. https://www.nature.com/articles/s41586-019-1622-4.*

Climate Change Affects Fungal Infectious Disease

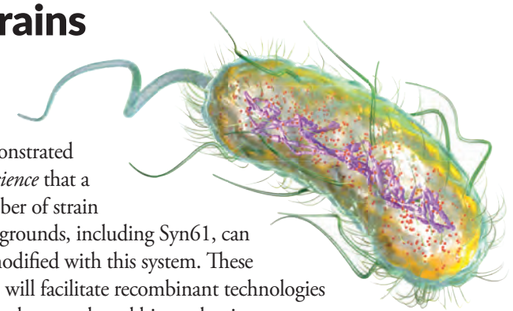


Climate change will alter many aspects of infectious disease, including the emergence of new pathogens and new niches for established pathogens. In an *mBio* article, several scientists recently suggested that rising global temperatures may select for environmental fungi that can grow at mammalian body temperatures, possibly contributing to the emergence of the fungal pathogen *Candida auris.* Phylogenetic analyses of *C. auris* suggest that several lineages emerged independently in geographically separated regions, with all lineages able to grow at elevated temperatures. The authors suggest that warming temperatures may be a common factor for these events, with the caveat that other factors are likely involved. Climate change may also affect the suitable environmental range for known fungal pathogens: Predictive models published in *GeoHealth* suggest that the climate permissive for *Coccidiodes*, an environmentally acquired human fungal pathogen, will spread from the southwestern U.S. throughout the Great Plains and Pacific Northwest. Concerns of increasing fungal pathogen numbers and environmental range were addressed in a recent American Academy of Microbiology Colloquia Report, in which experts recommend research funding increases and more training for early-career scientists in fungal pathogenesis fields.

- *Casadevall A., Kontoyiannis D.P., and Robert V. On the Emergence of* Candida auris: *Climate Change, Azoles, Swamps, and Birds.* mBio. *July 23, 2019. https://mbio.asm.org/content/10/4/e01397-19.*
- *Gorris M.E.*, et al. *Expansion of Coccidioidomycosis Endemic Regions in the United States in Response to Climate Change.* GeoHealth. *Aug. 30, 2019. https://agupubs.onlinelibrary.wiley.com/doi/10.1029/2019GH000209.*
- *Konopka J.B.*, et al. *One Health: Fungal Pathogens of Humans, Animals, and Plants. American Academy of Microbiology Colloquia Report. September 2019. https://www.asmscience.org/content/colloquia.56.*

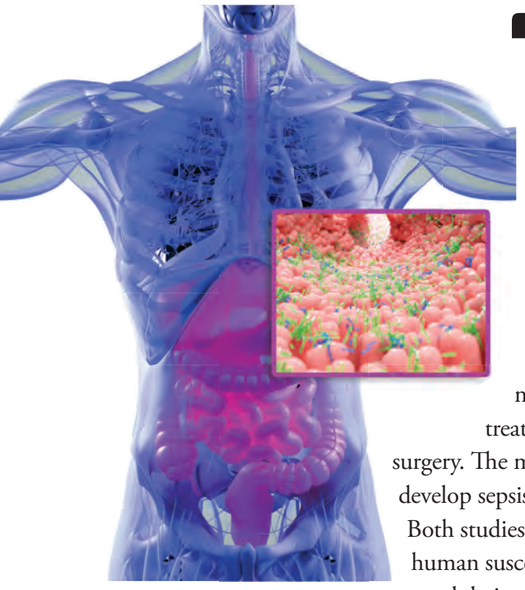
Expanding Synbio Tools and Strains

Synthetic biologists can now incorporate non-canonical amino acids and shuffle chromosomal segments more easily than ever. A new strain of *Escherichia coli* incorporates a rewritten genetic code that has a genome consisting of 61 codons instead of the natural 64 codons. The recoded genome required 18,214 codons to be replaced, and the new *E. coli* strain was dubbed Syn61 in a recent *Nature* article. Syn61 has a slightly longer doubling time and cells that are slightly elongated relative to the parental strain, but provides the opportunity to incorporate non-standard amino acids or other components through the now-unused codons. Moving around large sections of bacterial chromosomes became easier with programmable fission of the *E. coli* genome into engineered pairs of synthetic chromosomes coupled with the programmable, scarless fusion of synthetic chromosomes. These genetic manipulations don't require prior modifications in the *E. coli* genome, and the research team demonstrated in *Science* that a number of strain backgrounds, including Syn61, can be modified with this system. These tools will facilitate recombinant technologies for both research and bioproduction.



- *Fredens J.*, et al. *Total Synthesis of* Escherichia coli *with a Recoded Genome.* Nature. *May 15, 2019. https://www.nature.com/articles/s41586-019-1192-5.*
- *Wang K.*, et al. *Programmed Chromosome Fission and Fusion Enable Precise Large-Scale Genome Rearrangement and Assembly.* Science. *Aug. 30, 2019. https://science.sciencemag.org/content/365/6456/922.*

Gut Microbiome Influences Host Susceptibility to Disease



The gut microbiome has been shown to influence human disease susceptibility in some unexpected ways. A study conducted in human volunteers recently demonstrated that antibiotic therapy can decrease the efficacy of the influenza vaccine. The study, published in *Cell*, showed that the gut microbiome compositional changes in the antibiotic-treated cohort correlated with increased inflammatory signals in the blood and decreased neutralizing antibody titers, which are likely linked to loss of microbiome-produced secondary bile acids. A separate report in *mBio* showed that antibiotic disruption of gut microbial compositions also increased susceptibility to sepsis in a mouse model of infection. In the study, mice were fed a high-fat diet before treatment with or without antibiotics and subsequent liver resection surgery. The mice treated with antibiotics before surgery were more likely to develop sepsis due to dissemination of multidrug-resistant microbiome members. Both studies emphasize the importance of gut microbiome composition in human susceptibility to infectious diseases and the role that antibiotics play in modulating that composition and, by extension, human health. However, more studies are needed to determine how to best sample and measure a patient's microbiome for health assessments. This was shown in an *mSphere* report that demonstrated that rectal swab and stool samples from the same patients provide different representations of the gut microbiota present.

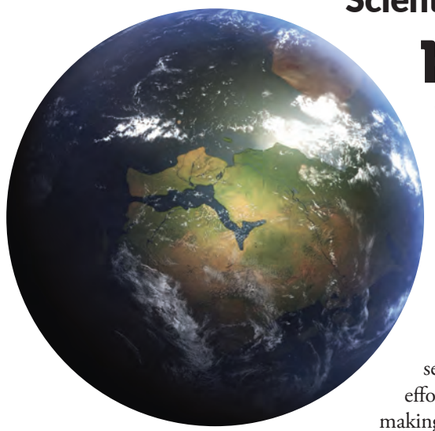
- *Hagen T.*, et al. *Antibiotics-Driven Gut Microbiome Perturbation Alters Immunity to Vaccines in Humans.* Cell. *Sept. 5, 2019. https://www.cell.com/cell/fulltext/S0092-8674(19)30898-0.*
- *Hyoju S.K.*, et al. *Mice Fed an Obesogenic Western Diet, Administered Antibiotics, and Subjected to a Sterile Surgical Procedure Develop Lethal Septicemia with Multidrug-Resistant Pathobionts.* mBio. *July 30, 2019. https://mbio.asm.org/content/10/4/e00903-19.*
- *Fair K.*, et al. *Rectal Swabs from Critically Ill Patients Provide Discordant Representations of the Gut Microbiome Compared to Stool Samples.* mSphere. *July 24, 2019. https://msphere.asm.org/content/4/4/e00358-19.*

New Viruses of Human Microbiome and More

Advances in metagenomic sequencing technologies have facilitated the discovery of new viruses of the human microbiome. A study published in *Cell Host & Microbe* announced the *Redondoviridae*, a new family of circular Rep-encoding single-stranded (CRESS) viruses identified via homology of the viral Rep gene to related sequences. Subsequent searches in metagenomic datasets revealed the virus to be human-specific and pointed to a possible role in disease based on higher-sequence abundance in periodontitis patients that decreased with treatment. A separate *Nature Microbiology* article reported the origin, evolution and epidemiology of *crAssphage*, a widespread human gut bacteriophage discovered in 2014. Though *crAssphage* has no clear associations with health or disease, *crAssphage*-like genomes in primates suggest that the virus-host association may be millions of years old. Discovery of these new mammalian viruses is unlikely to plateau in the near future, as a *Nature Ecology & Evolution* article reports that there are likely 40,000 virus species in mammals. This estimate, based on a model that incorporates host-sharing, is two logs lower than previous estimates but still leaves much to be explored in the viral world.

- *Abbas A.A.*, et al. *Redondoviriae, a Family of Small, Circular DNA Viruses of the Human Oro-Respiratory Tract Associated with Periodontitis and Critical Illness.* Cell Host & Microbe. *May 8, 2019. https://www.cell.com/cell-host-microbe/pdfExtended/S1931-3128(19)30171-4.*
- *Edwards R.A.*, et al. *Global Phylogeography and Ancient Evolution of the Widespread Human Gut Virus* crAssphage. Nature Microbiology. *July 8, 2019. https://www.nature.com/articles/s41564-019-0494-6.*
- *Carlson C.J.*, et al. *Global Estimates of Mammalian Viral Diversity Accounting for Host Sharing.* Nature Ecology & Evolution. *June 10,2019.https://www.nature.com/articles/s41559-019-0910-6.*

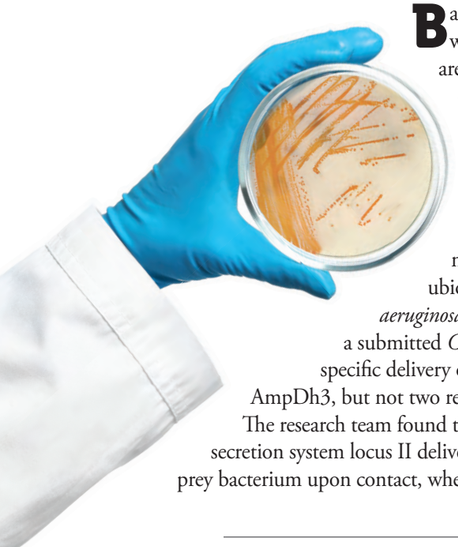
Scientists Discover Clues to Life on Early Earth



How did life originate? Scientists grew closer to answering this question with the discovery of a *Lokiarchaeota*-related *Asgard archaeon* from deep marine sediment, an effort 10 years in the making. *Candidatus Prometheoarchaeum synthrophicum* strain MK-D1 is the first isolated member of the *Asgardarchaeota*, which is posited to be the archaeal lineage most closely related to the eukaryotes. Scientists hope that studying the slow-growing archaeon, announced on *bioRxiv,* will provide insight into the origins of complex life. A second study looks even further back in history to the production of the first biological molecules from nonbiological precursors. The RNA world hypothesis posits that RNA was the first biological molecule, but previous studies had shown that pyrimidines and purines required different chemical synthesis pathways. Now a study in *Science* reveals a one-pot recipe for the RNA nucleobases driven by wet-dry cycling under conditions similar to those of early Earth. The studies offer hints about the emergence of life as we know it.

- *Imachi H.*, et al. *Isolation of an Archaeon at the Prokaryote-Eukaryote Interface.* bioRxiv. *Aug. 8, 2019. https://www.biorxiv.org/content/10.1101/726976v2.*
- *Becker S.*, et al. *Unified Prebiotically Plausible Synthesis of Pyrimidine and Purine RNA Ribonucleotides.* Science. *Oct. 4, 2019. https://science.sciencemag.org/content/366/6461/76/.*

Can't We All Just Get Along? (No)



Bacterial relationships with their neighbors are complex, and competitors for similar niches have devised clever schemes to gain the upper hand. A new competitive mechanism of the ubiquitous *Pseudomonas aeruginosa* was described in a submitted *Cell Reports* article: specific delivery of the zinc protease AmpDh3, but not two related zinc proteases. The research team found that the type VI secretion system locus II delivers AmpDh3 to the prey bacterium upon contact, where the enzyme breaks down the cell-wall peptidoglycan, promoting prey bacterium death. In another competitive interaction, *Streptococcus pneumoniae* is known to kill *Staphylococcus aureus* by the production of hydrogen peroxide. A *Journal of Bacteriology* report demonstrates that *S. pneumoniae* enzymes SpxB and LctO produce hydrogen peroxide, which is converted into a hydroxyl radical that intoxicates and kills *S. aureus*. These mechanisms provide a competitive advantage to the bacteria that use them and may provide insight into molecular targets for antimicrobial compound development.

- *Wang T.*, et al. *The Type VI Secretion System of* Pseudomonas aeruginosa *Delivers a Cell-Wall Amidase to Target Bacterial Competitors.* Cell Reports. *Aug. 27, 2019. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3443148.*

- *Wu X.*, et al. *Interaction between* Streptococcus pneumoniae *and* Staphylococcus aureus *Generates OH Radicals that Rapidly Kill* Staphylococcus aureus *Strains.* Journal of Bacteriology. *Oct. 4, 2019. https://jb.asm.org/content/201/21/e00474-19.*

Measuring Dietary Effects on the Gut Microbiome

Scientists are learning more about how the food we eat affects the composition of the gut microbiome. A *Cell Host & Microbe* study examined the effect of processed foods, specifically the effect of maillard reaction products (MRPs) that are commonly found in processed foods. The research team found that dietary whey protein increases the abundance of specific *Collinsella* species based on their ability to catabolize fructoselysine, an MRP that results from the reaction of glucose and whey. This is applicable to people eating a Western diet, who ingest 500-1275 mg per day of MRPs. Tracking the exact components responsible for changes in the microbiome composition and function may become easier based on DNA tracking of dietary intake. Researchers applied DNA metabarcoding to evaluate the plant components of human diets from stool samples; their results aligned closely with the foods listed in the diaries kept by study participants. The scientific team suggests that this method may also be able to track dietary fungal and animal products, which may make stool a one-stop shop to evaluate dietary intake and microbiome alterations from a single sample.

- *Wolf A.R.*, et al. *Bioremediation of a Common Product of Food Processing by a Human Gut Bacterium.* Cell Host & Microbe. *Oct. 9, 2019. https://www.sciencedirect.com/science/article/pii/S1931312819304688.*

- *Reese A.T.*, et al. *Using DNA Metabarcoding to Evaluate the Plant Component of Human Diets: A Proof of Concept.* mSystems. *Oct. 8, 2019. https://msystems.asm.org/content/4/5/e00458-19.*

Room for Improvement with Antibiotic Stewardship in Outpatient Settings

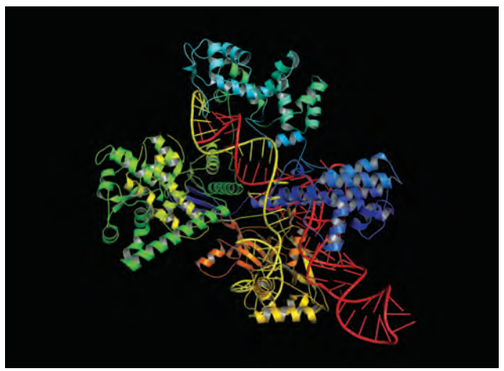
Several studies have demonstrated room for improvement in antibiotic selection in outpatient settings, where more than 60% of antibiotic expenditures are made, according to the Centers for Disease Control and Prevention. An *Antimicrobial Agents and Chemotherapy* study reports that only 50% of patients at physicians' offices receive first-line treatments — those recommended by medical guidelines — while that number is 70% of patients at retail clinics, 57% at emergency departments and 49% at urgent care centers. The goal is to administer 80% of patients a first-line treatment. Retail clinics have higher emphasis on protocol auditing and feedback, which Senior Author Katherine E. Fleming-Dutra credited to a higher percentage of retail clinics following correct guidelines. A more targeted study published in *Clinical Therapeutics* found similarly low numbers among patients diagnosed with community-acquired pneumonia. Of 341 diagnosed outpatients included in the study, nearly 70% did not receive an antibiotic regimen consistent with guidelines. Both studies were performed in the U.S.

- *Palms D.L.*, et al. *First-Line Antibiotic Selection in Outpatient Settings.* Antimicrobial Agents and Chemotherapy. *Sept. 23, 2019. https://aac.asm.org/content/early/2019/08/27/AAC.01060-19?_ga=2.7306930.1492542486.1571061598-754189529.1560784661.*

- *Wattengel B.A.*, et al. *Outpatient Antimicrobial Stewardship: Targets for Community-Acquired Pneumonia.* Clinical Therapeutics. *Feb. 7, 2019. https://www.clinicaltherapeutics.com/article/S0149-2918(19)30011-6/fulltext.*

New Arsenals to Direct the Fight Against AMR

Antimicrobial resistance (AMR) continues to spread, requiring new methods to attack AMR microorganisms causing infection. An *Antimicrobial Agents and Chemotherapy*



article reported on a cutting-edge application of CRISPR-Cas9 technology to combat AMR. In the study, a pheromone-responsive conjugative plasmid was transferred efficiently into the gut bacterium *Enterococcus faecalis* to deliver a CRISPR-Cas9 that specifically targets resistance determinants carried by AMR bacteria. The authors demonstrate that the tool depleted AMR *E. faecalis* carried in a mouse model, and protected mice against the uptake of resistance determinants by their commensal bacteria. A second study published in *bioRxiv* may help establish which genetic determinants warrant targeting. The authors compiled all available bacterial genomes, plasmids, integrons and 850 metagenomes to rank the risk of antimicrobial resistance genes (ARGs) based on "anthropogenic enrichment," "mobility" and "host pathogenicity." The team validated their list using a list of high-risk ARGs from the World Health Organization, and used their list to determine effective interventions to stop the spread of the ARGs.

- *Rodrigues M.*, et al. *Conjugative Delivery of CRISPR-Cas9 for the Selective Depletion of Antibiotic-Resistant* Enterococci. Antimicrobial Agents and Chemotherapy. *Sept. 16, 2019. https://aac.asm.org/content/aac/early/2019/09/05/AAC.01454-19.full.pdf?ijkey=zcyC3I9YGXIXU&keytype=ref&siteid=asmjournals&_ga=2.106353667.1492542486.1571061598-754189529.1560784661.*

- *Zhang A.N.*, et al. *Choosing Your Battles: Which Resistance Genes Warrant Global Action?* bioRxiv. *Oct. 3, 2019. https://www.biorxiv.org/content/10.1101/784322v1.full.*

Most Popular Articles

Get Even More Microbiology at asm.org

by Julie Wolf, Ph.D.

Every week, asm.org features new articles that cover all aspects of the microbial sciences. Here are some of our most popular 2019 articles, in no particular order, available online only:

The Frozen Potential of Microbial Collections

asm.org/MicrobialCollections

Why do we collect? Collections are based on a conviction that, even beyond a human lifetime, they will provide value to the next generation. This is especially true when an entire field of science bands together to amass organisms of interest for posterity. Brian Lovett discusses what microbial collections are, how they are maintained and what their role is to the greater scientific community.

Microbiomes: An Origin Story

asm.org/MicrobiomeOrigins

Many people assume that Nobel Laureate and microbiologist Joshua Lederberg first coined the term "microbiome" in 2001, but Janet Goins, Ph.D., demonstrates that the term was published years earlier. Microbial ecologists have been encouraging the study of microbial interactions in their natural environments since the time of Sergei Winogradsky, one of the first to build natural-environment culturing devices. Goins explains Winogradsky's work, how it informed the famous Winogradsky column and how the history of microbiome research continues to influence today's scientists.

Poop, Pus and Positive Results: Cultural Oddities from the Clinical Microbiology Lab

asm.org/CulturalOddities

Although clinical microbiologists laugh about the unusual things that occur during specimen collection or result interpretation, the proper execution of both components of the diagnostic process is critical to quality patient care. It is the job of the clinical microbiologist to ensure they happen correctly. Andrea Prinzi, SM(ASCP), M.PH., CPH, shares humorous (and sometimes horrific) stories of unusual sampling protocols, along with educational tips to apply the next time these situations arise.

The 7 Viruses that Cause Human Cancers

asm.org/7Viruses

Compared to other viruses, human tumor viruses are unusual because they infect, but do not kill, their host cells. Viral infection can lead to cancer through a number of mechanisms; human tumor viruses account for an estimated 12% to 20% of cancers worldwide. Jennifer Brubaker, M.S., summarizes the seven known oncogenic viruses and the major cancers associated with each.

Who Are the HACEK Organisms?

asm.org/MicrobialCollections

Although most notable for causing infective endocarditis, the HACEK organisms (*Haemophilus, Aggregatibacter, Cardiobacterium, Eikenella* and *Kingella*) are significant causes of other diseases, including periodontitis, abscesses and septic arthritis. All HACEK members are fastidious Gram-negative bacteria that comprise commensal organisms of the human oropharynx. K.P. Smith, Ph.D., provides the historical significance and modern diagnostic techniques used for these difficult-to-identify organisms.

Snow Is Coming — What's That Have to Do with Microbes?

asm.org/SnowIsComing

Do bacteria help form clouds? How would a scientific team demonstrate this? How long would this take? Jennifer Tsang, Ph.D., tells the story of David Sands' decades-long research on *Pseudomonas syringae* in cloud and precipitation formation and the ice-nucleating protein whose mechanism wasn't discovered until 20 years later.

Measles Vaccination and Infection: Questions and Misconceptions

asm.org/MeaslesVaccineFAQ

The recent measles outbreaks in the U.S. are different from those that occurred regularly in the pre-vaccine era because they are happening within a highly vaccinated population. This results in potential confusion for the public and in complications for physicians, epidemiologists and clinical microbiology labs working to identify infected patients and to track and control the outbreaks. Thea Brennan-Krohn, M.D., D(ABMM), explores some common sources of confusion and misconceptions about the current measles outbreak in the U.S. and similar epidemics in populations where most people have been vaccinated.

Notorious C.R.E.: Promising Mass Spectrometry Diagnostics for Detecting Antimicrobial Resistance

asm.org/NotoriousCRE

Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) has revolutionized clinical microbiology diagnostics with its ability to identify microbial organisms in a matter of seconds. Lisa Leung, Ph.D., summarizes the current state of MALDI-TOF research for detecting antibiotic resistance, as well as organism ID, plus what the future holds for this technology.

C. diff Diagnosis Versus Detection: Why Tests Remain Ambiguous

asm.org/CdiffDiagnosis

There is significant confusion regarding clinical interpretation and the distinction between colonization and true infection with *Clostridioides difficile*. This confusion results from the multitude of tests available for *C. difficile* diagnosis. Rose Lee, M.D., expertly breaks down the diagnostic strategies and limitations of toxin detection, culture, glutamate dehydrogenase detection, nucleic acid amplification tests and algorithm-based multistep testing for *C. difficile* infection.

Paleomicrobiology and Microbial Ancient DNA Get to the Root of Disease Mysteries

asm.org/Paleomicrobiology

Paleomicrobiology is a fascinating branch of science borne from multiple disciplines, including microbiology, anthropology, history, paleontology and archaeology. The field relies heavily on the analysis of microbial ancient DNA to diagnose past infectious diseases and analyze the virulence, evolution and lifestyles of ancient pathogens. Ashley Hagen, M.S., explains what ancient DNA is, where it is found and some of the mysteries microbial ancient DNA has helped solve.

What's New at ASM

ASM Press Launches Publishing Partnership with Wiley

ASM Press will begin an exciting new partnership with commercial publisher Wiley, a global leader in research and education. The partnership aims to increase the impact and relevance of ASM's non-journal content. ASM and Wiley will also create an online reference that will make ASM's gold standard clinical microbiology content highly searchable and updated as the practice changes.

The ASM team has chosen to work with Wiley because of its commitment to nurturing society partnerships. Through this partnership, Wiley aims to transform ASM's information, knowledge and learning publishing to reach more scientists, clinicians and students globally and to extend ASM's reach into the higher education and library markets.

What Is Changing

Wiley is now the official co-publisher and distributor of ASM Press titles and is now selling and distributing 70 of ASM Press's best-selling and recent books in print and as ebooks. Wiley and ASM will co-publish all books beginning with the 2020 copyright year. In the near future, access to the ebooks collections sold to libraries will shift from ASMscience to Wiley Online Library.

What Is Staying the Same

ASM Press staff will still work directly with authors and editors to receive, review and develop content into its final form for publication. We value our close relationships with experts in the microbial sciences.

ASM Partners with CDC to Combat Antibiotic Resistance

To celebrate the success of the Antimicrobial Resistance (AMR) Challenge, ASM cohosted an event in partnership with the Bill & Melinda Gates Foundation, Wellcome Trust, Antimicrobial Resistance Fighter Coalition and the CDC Foundation. "A Night Celebrating Antimicrobial Resistance Fighters," a side event at the 2019 United Nations General Assembly, showcased how AMR is impacting our world. This multi-media art experience featured art installations, four pieces from ASM's award-winning agar art and the U.S. premier of the "Antimicrobial Resistance Fighters" documentary, which highlighted the impact of antibiotic resistance on the world and the need for greater awareness. ASM joins nearly 350 One Health commitments made by governments, non-government organizations and academic and private sector partners to take action and deliver results.

(Left to right) ASM President Robin Patel, U.S. Department of Health and Human Services Secretary Alex Azar and ASM CEO Stefano Bertuzzi.

ASM Advocates for Science During Hill Day

ASM leaders with Congresswoman Susan Brooks.

ASM's Public and Scientific Affairs Committee (PSAC) leaders took to Capitol Hill recently to promote issues relating to science. The committee members informed a bipartisan selection of legislators and their staffs about using ASM as a resource, supporting vaccines and funding microbial research. This meeting was just a first step in ASM's efforts to encourage more microbiologists to make their voices heard and advocate for better science policy.

If you don't know what to expect when meeting with your Representative or Senators, a visit to their offices can feel very intimidating. However, developing a connection with your legislators is a great way to spread information on your science. Melissa B. Miller, Ph.D., D(ABMM), F(AAM) of The University of North Carolina School of Medicine, Chapel Hill, who had her first meetings on the Hill, said that "the most meaningful [part] for me was to establish a relationship with my representative's and senators' offices so there can be a continued dialogue. I hope they will come visit our lab next time they are in North Carolina!"

On Hill Day, ASM recognized Rep. Anna Eshoo (D-Calif.) and Rep. Susan Brooks (R-Ind.), who co-chair the Congressional Biodefense Caucus and successfully led the House effort to reauthorize the Pandemic and All-Hazards Preparedness and Innovation Act (PAHPA). Passage of PAHPA was a priority for ASM this past year.

Scientists everywhere have the opportunity to share their expertise with lawmakers. Doing so helps make ties between policy and science stronger, therefore bringing about legislation that can better reflect the needs of the scientific community.

ASM leaders with Congresswoman Anna Eshoo.

Triinu Visnapuu, Ph.D.

Triinu Visnapuu, Ph.D., from the Institute of Molecular and Cell Biology, University of Tartu, Tartu, Estonia, has been an ASM member since 2014 and became the Young Ambassador to Estonia in 2018.

Triinu is a board member of the Estonian Society for Microbiology, the Delegate of Estonia on the Federation of European Microbiological Societies (FEMS) Board and the FEMS Grants Board. She teaches a practical course in microbiology and virology in Estonian and in English at the University of Tartu.

Tell us more about your work on developing the field of microbiology at national and European organizations.

I did my postdoc at Technical University of Denmark at the lab of Prof. Birte Svensson, where I studied bacterial enzymes, potentially used for synthesis of oligosaccharides similar to ones found in milk. I currently work as a researcher in microbial glycobiotechnology at the University of Tartu. My work focuses on connecting the aspects of microbial enzymes, glycobiology (biology of saccharides or sugars) and biotechnology. Our group has been investigating carbohydrate-active enzymes from so-called nonconventional yeasts *Ogataea polymorpha* and *Blastobotrys (Arxyla) adeninivorans* and from various bacterial species. Our research specifically focuses on α-glucosidases (*e.g.,* maltases) from yeasts and biopolymer levan-synthesizing and -degrading enzymes (levansucrases, levanases).

We have addressed issues of how enzymatically produced carbohydrates modulate fecal microbiota and investigated other properties with the biotechnological value of these sugars. I'm currently working on a project with the aim of immobilizing these microbial enzymes to different carriers to repeatedly and more efficiently use the catalyst.

What's your favorite event or activity you've run as an ASM Ambassador?

Compared to other life sciences and technological disciplines among STEM, microbiology is underrepresented in science outreach activities and K-12 education. For Europe's International Microorganism Day 2018, I collaborated with ASM and my colleagues from the University of Tartu, University of Life Sciences, Tallinn University of Technology and the National Institute of Chemical Physics and Biophysics to create an outreach event for high school students. We had short presentations from early career scientists, live connections to similar events in Europe and exhibitions by universities and companies. We also hosted hands-on workshops, including an agar art workshop sponsored by ASM. Our event inspired the Estonian Healthcare Museum to launch the exhibition "Me, Superorganism" on human microbiota.

What did you love most about the Women in Science (WiSci) Girls STEAM Camp held in Tallinn, Estonia, in July 2019?

I loved the supportive and friendly atmosphere. The Women in Science (WiSci) Girls STEAM Camp in Tallinn gathered approximately 100 girls from the United States, Estonia, Poland, Latvia and Georgia, who had two intensive weeks of lectures, workshops and visits related to Science, Technology, Engineering, Arts and Design, and Mathematics (STEAM) subjects *(see page 11)*. I was a local expert and supervisor for ASM's microbiology workshop, which was very successful thanks to ASM program coordinator Alexis Rose. We incorporated Foldscopes and colorful agar art to demonstrate the magnificent world of microbes. We ended with a nice discussion on careers in microbiology.

ASM Program Coordinator Alexis Rose (left) with ASM Young Ambassador Triinu Visnapuu, Ph.D. (right) during WiSci Estonia 2019.

Describe your experience as a woman in STEM.

The gender gap in life sciences in Estonia has been rather minor. There are more female students than males in undergraduate studies. However, not many female scientists reach the professor and group-leader level for various reasons. I personally received strong support from my supervisors and professors and my supervisors for my Ph.D. thesis and postdoctoral work were females.

What are your plans as an Ambassador for 2020?

Next year I plan to organize a larger outreach/K-12 education event on International Microorganism Day. I will also continue developing and supervising agar art workshops. I would like to focus more on undergraduates and early-career scientists. Based on what I've heard from my fellow ASM Ambassadors, poster prizes, dedicated workshops and career talks at national or regional conferences are great ways to achieve this.

My journey as an ASM Young Ambassador has been very exciting, providing new opportunities and new perspectives in microbiology. It has been an excellent opportunity to network with active and bright ASM Young Ambassadors from so many countries.

The Allegheny Branch

The Allegheny Branch originated in April 1934 as the Central Pennsylvania Section of the Society of American Bacteriologists. A group at Penn State University created the Branch, with Dr. J.A. Sperry serving as its first president. In 1948, 75 people attended a meeting for the renamed Allegheny Branch of the Society of American Bacteriologists and elected the following officers: Michael A. Farrell, President; Jonas E. Salk, President-elect; John C. Garey, Secretary Treasurer; and Mary Aiken, Councilor. In 1961, the Branch officially changed its name to the Allegheny Branch of the American Society for Microbiology (ABASM).

Historically, ABASM hosted biannual meetings, with the exception of an inactive period during the World War II era. Currently, ABASM meets annually in November. Most members are affiliated with educational organizations, so Branch meetings are rotated among member institutions. In recent years, ABASM hosted meetings at the University of Pittsburgh-Greensburg (2015), Penn State-Behrand (2016), Juniata College (2017) and Gettysburg College (2018). St. Francis University will host the 2019 annual meeting.

ABASM meeting at Gettysburg College.

Workshop attendees view a flow-through cell with microbial biofilm build-up from a hay infusion.

John Lennox from Penn State Altoona hosted a biofilm workshop during the 2012 ABASM meeting.

ABASM is very interested in clinical, industrial and other microbiological fields. Branch meetings focus on best practices in microbiology education and the presentation of student research in microbial sciences, particularly undergraduate work. Typically, 100-125 people attend Branch meetings, and approximately 85% of attendees are students and trainees. Monetary prizes for oral and poster presentations are highly competitive among undergraduates. The ASM Distinguished Lecturer keynote and professional development workshops for students (*e.g.,* career panels on diverse careers available to microbiologists) and faculty (*e.g.,* how to practice inclusive pedagogy in their classrooms) are always highlights of the meeting.

One of the most notable ABASM members is Dr. Jonas E. Salk, an American medical researcher and virologist. He discovered and developed one of the first successful polio vaccines.

For more information, visit: http://www.asmbranches.org/brAllegheny/

Microcosm will be highlighting one ASM branch in each issue. If your branch would like to be featured, please send a high-resolution photo and information on your branch's history, members, activities, student chapter and website to **communications@asmusa.org**