Despite Good Vaccines, Some Childhood Diseases Present Challenges

Jeffrey L. Fox

Several childhood diseases that supposedly disappeared are resurgent, while others show signs of yielding at long last to analysis and novel interventions, according to several investigators who presented their findings during the 2013 Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Denver, Colo., last September. Diseases and syndromes in question include pertussis, mumps, polio, and toxic shock syndrome (TSS).

In 2012, parts of Minnesota experienced the “largest regional outbreak of pertussis in recent history,” says Alexander Theofiles of Mayo Clinic in Rochester, Minn. “Of those with positive tests, the average age was 14 years.” All in all, the findings “suggest decreased efficacy of the acellular compared to whole-cell killed vaccines.”

That localized outbreak comes amid a “huge increase” in pertussis among older adults throughout the country, with the incidence perhaps as high as 464 per 100,000 among adults 65 and older, according to Cristina Masseria of GlaxoSmithKline Vaccines in King of Prussia, Pa. "Typically, pertussis infections are "not very severe in adults, [who] unknowingly spread pertussis to infants."

However, this rise in pertussis infections is not limited to the elderly, it is also occurring among children aged 5 to 11, particularly after the United States and other countries moved from using a whole-cell to subunit versions of the vaccine, which have fewer side effects, says Roger Baxter, Kaiser Permanente Vaccine Study Center in Oakland, Calif. “Most children have five doses of the pertussis [subunit] vaccine by age 5, but, by age 10, immunity wanes in kids who got it.” He recommends using adjuvants to improve the immune response, hopefully without adding to the “reactogenicity” of the subunit vaccine.

Like pertussis, mumps is also on the rise in several countries, including South Korea and Canada. During the past 3 years, outbreaks of mumps occurred mainly among high school students in South Korea, despite high vaccine coverage, according to Young June Choe of National University Hospital in Seoul, Republic of Korea. About half the cases were aged 14 to 17 years, he says. Because military service is mandatory for men in South Korea, the government can cover at least half the vulnerable young-adult population by revaccinating them as they enlist, he points out.

In Canada, however, reaching this same-age cohort is a major challenge, according to Noni McDonald of Dalhousie University in Halifax, Nova Scotia, Canada. “Why have we failed to eliminate mumps?” she asks. “We have a great vaccine.” Part of the reason is that a single or even double dose might not be enough. Moreover, the vaccine was modified several times to reduce side effects, and those changes appear to have lowered its efficacy. Yet another problem is that young adults, who appear to be most at risk, are not inclined to respond to invitations that they be revaccinated, she laments. “I suggested

Colored transmission electron micrograph of a mumps virus particle (at center left). Mumps, one of several diseases that formerly had been effectively controlled by vaccination, has recently been appearing in young adults in South Korea and Canada. (Image © Eye of Science/Science Source.)
that we give them the vaccine at bars, but was laughed at.” Yet, the close quarters in bars where some college-age young adults congregate are a prime environment in which the mumps virus is passing among infected and other susceptible individuals. “It’s not some weirdo new viral strain, but decreases in mumps antibodies with time” that explain recent outbreaks, she adds. “Maybe we need to give everyone a third dose.”

Although polio infections continue to decline thanks to international efforts to vaccinate children, eradication of this disease will “require antiviral drugs,” as part of a mop-up operation, particularly to treat cases that arise from disease-causing mutants of the widely used live-virus, oral vaccine, according to Mark Collett of ViroDefense, Inc. in Rockville, Md. To test one such candidate drug, pocapavir, he and his collaborators recently conducted a clinical trial in Sweden, one of the few countries in which health officials rely exclusively on the killed-virus vaccine to protect the population against this disease.

In the trial, vaccinated adults were challenged with the live-virus vaccine and then treated with either pocapavir or a placebo. Oddly, almost exactly half those treated with the drug responded to it, based on analysis of poliovirus levels (from the oral vaccine challenge) in fecal samples, according to Collett. Those titers dropped by a log per day for three days among responders, whereas the fecal virus levels from non-responders looked like those in the placebo group, he says. The pattern of resistance is “very different from what’s seen in outbreaks caused by natural polio viruses in field studies,” he adds. In part for such reasons, the company is developing another antiviral drug candidate with a different mechanism and different resistance profile.

Meanwhile, despite a generally held belief, toxic shock syndrome (TSS) “didn’t go away,” says James Todd of the University of Colorado School of Medicine in Denver. Indeed, TSS not only occurs in both men and women but also among young children and adolescents, and is important to recognize in that population, he says. “Human genotype plays a role in the response,” he adds, noting that individuals who fall into particular major histocompatibility groups tend to “over-respond” to TSS.

Meningococcal disease in infants can be just as devastating as TSS—beginning with rash and fever before “everything goes wrong,” with a mortality rate as high as 20%, says Michael Levin of Imperial College in London, United Kingdom. As many as four blood-clotting pathways can become “deranged,” leading to a “profound imbalance of clotting.” Recent analysis indicates that host cell-secreted interleukin-6 is a key factor in that end-stage response, and it might be possible to rescue patients with drugs that block its effects, he adds.

ASM MEETINGS: 2013 ICAAC Noninvasive Testing for Fungal Infections Via Metabolomics Shannon Weiman Telltale metabolites may unveil pathogens that otherwise would be difficult to diagnose when they are causing infections, according to several researchers who presented findings at the 2013 Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), held in Denver last September. Metabolites in saliva or expelled with each breath might serve as the basis for noninvasive diagnostics of fungal or other infectious diseases, they point out. Moreover, ease in collecting and analyzing such samples would make such diagnostic tests particularly useful in pediatric, geriatric, and veterinary medicine, as well as for use as point-of-care-diagnostics in hospitals and rural settings or in developing nations.

“Metabolic profiles of biofluid can be altered by a variety of physiological and pathological processes, and . . . may signal the presence of a particular disease state,” says Mahmoud Ghanenour of Case Western Reserve University in Cleveland, Ohio, and Chairman of the Oral HIV AIDS Research Alliance (OHARA), who spoke during
MINITOPIC
CDC Urges Four “Core Actions” against Antibiotic Resistance

The report “Antibiotic Resistance Threats in the United States, 2013” presents the “first snapshot of the burden and threats posed by antibiotic-resistant germs having the most impact on human health,” according to officials of the Centers for Disease Control and Prevention (CDC) in Atlanta, Ga., who released that report last September. “Antibiotic resistance is rising for many different pathogens that are threats to health,” says CDC Director Tom Frieden. “If we don’t act now, our medicine cabinet will be empty, and we won’t have the antibiotics we need to save lives.” In addition to exacting a toll on human life, antibiotic-resistant infections add considerable costs to health care systems in the United States (U.S.) and elsewhere. In the U.S., for example, antibiotic resistance adds an estimated $20 billion in excess direct health care costs, with additional costs to society for lost productivity totaling up to $35 billion a year, according to agency officials. With as much as 50% of prescribed antibiotics not needed or not prescribed appropriately, the use of such drugs “is the single most important factor leading to resistance,” they note. The report identifies four core actions to fight antibiotic resistance: preventing infections and the spread of resistance, tracking resistance patterns, improving use of antibiotics, also called antibiotic stewardship, and developing new antibiotics and diagnostic tests.

The symposium “Fungi-Omics: Highlighting Recent Advances.” In many cases, what can be found in saliva accurately reflects the metabolic status of other tissues in the body that are more difficult and potentially dangerous to sample, he says. “Most of the biomarkers present in blood and urine can also be detected in a sample of saliva.” Indeed, salivary metabolomic tests are being developed for various medical conditions, including malignancies, cardiovascular disease, and infections.

Ghannoum identified a salivary metabolic signature for patients with oral candidiasis (OC), which may also be useful for identifying invasive infections of Candida albicans, he says. Specifically, OC changes six characteristic carbohydrate metabolites, distinguishing it from other oral infections involving fungal or bacterial pathogens. In vitro experiments indicate that C. albicans may produce these metabolites after interacting with epithelial cells in the mouth, as C. albicans cultured in the absence of these cells exhibits a different metabolic profile.

Similarly, detection of pathogen-specific volatile metabolites in patient breath can be used to diagnose specific infectious diseases, according to Sophia Koo of Brigham & Women’s Hospital in Boston, Mass., who presented her findings during the poster session “Clinical Mycology.”

Koo is developing a breath test for invasive aspergillosis, a common fungal disease that is difficult to diagnose because conventional tests can be inconclusive and patients suspected to have these infections may require invasive and potentially dangerous diagnostic procedures such as biopsies. An accurate, rapid, and noninvasive test for invasive aspergillosis could potentially reduce mortality rates among infected patients, which can exceed 60%, she says.

Building on in vitro studies, where she and her collaborators identified a species-specific volatile metabolite profile of farnesene and other terpenes and sesquiterpenes emitted by Aspergillus fumigatus, she analyzed breath samples from patients suspected to have Aspergillus lung infections and found that a combination of three Aspergillus fumigatus metabolites distinguished patients with invasive aspergillosis from those with other fungal or bacterial pneumonia, with an overall accuracy of 94%. She is expanding this work to profile volatile metabolites associated with other agents of pneumonia, hoping to develop a comprehensive breath test for lung infections.

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RESEARCH ADVANCES

Bacteria, Phages Share Needle-Like Virulence Proteins

Marcia Stone

PAAR (proline-alanine-alanine-arginine) repeat proteins sharpen the ends of phage-like bacterial spikes known as type VI secretion systems (T6SS)—serving as “needles” for these complex organelles through which gram-negative bacteria inject toxins into host cells during infection, according to Petr G. Leiman at École Polytechnique Fédérale de Lausanne in Switzerland and colleagues there as well as in the United States and Russia. Remarkably, phages encode and deploy nearly identical proteins to punch through the membranes of their bacterial host cells. Details appeared August 15, 2013 in Nature (500:350–353).

The sixth of seven bacterial secretion systems so far identified, T6SS is widely distributed and determines the virulence of various gram-negative pathogens, including Vibrio cholerae, Francisella tularensis, and Burkholderia mallei, according to Leiman. T6SS genes are clustered in pathogenicity islands and encode a version of VgrG (valine-glycine repeat protein) that sits on the tube’s distal end and secures the piercing tip. With phage contractile tail protein-coding genes as a guide, Leiman and collaborators identified PAAR repeat group proteins in both
phages and T6SS systems. The phage version is gp (gene product) 5.4, one of the smallest proteins encoded within the T4 genome, “which might explain why its function was unknown for such a long time,” he says. Both T4 and VgrG spikes have blunt ends, “thus we speculated that this was where the PAAR protein binds,” he adds.

Because VgrG proteins are insoluble, they were cut up and the fragments placed onto a T4 gp5 protein, enabling use of the phage spike for binding PAAR proteins, according to Leiman’s collaborator Mikhail M. Shneider from the Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry in Moscow. The PAAR proteins fold into very sharp symmetrical cone-shaped structures that fit perfectly onto VgrG spikes, he says. Because PAAR proteins use binding sites at the tip of VgrG spikes, these researchers predict that other toxins also use the PAAR domain to bind VgrG spikes before being translocated into target cells. “Thus, our findings support a new model for the T6SS in which a needle-sharp spike is decorated by multiple effectors that are delivered simultaneously into a target cell in a single contraction-driven translocation event,” Leiman says.

“This is a beautiful story,” says Karla J. F. Satchell at the Northwestern University medical school campus in Chicago, Ill., who was not involved in the research. Most intriguing, she says, is that these pathogens carry multiple copies of partly interchangeable PAAR proteins, possibly fine-tuned to match specific T6SSs—thus PAAR proteins might be prey specific. “Also of great interest is that bacteria seem to have successfully co-opted a system originally designed for predation by phage, and the two remain so tightly linked that a chimera is biochemically more stable than the native VgrG protein.”

“Remarkably, contractile tail-like systems can penetrate both bacterial and eukaryotic cell envelopes, suggesting that the underlying principle of creating a membrane channel for protein and DNA translocation must be universal,” says John J. Mekalanos of Harvard Medical School in Boston, Mass. “Understanding how these closely related tail-like organelles perform similar but clearly distinct tasks will provide fascinating insights into both the evolutionary process and the function and regulation of complex nanomachines.”

Marcia Stone is a science journalist based in New York, N.Y.

RESEARCH ADVANCES

Genomic Analysis Assigns Sea Anemone Unseen Bacterial Consorts

David C. Holzman

Genomic analysis of the starlet sea anemone Nematostella vectensis reveals that a substantial portion of its genes are more similar to bacterial and bacteriophage than to eukaryotic genes, according to Irena I. Artamonova of the N.I. Vavilov Institute of General Genetics RAS in Moscow, Russia, and Arcady Mushegian then at the Stowers Institute for Medical Research in Kansas City, Mo., and now at the National Science Foundation in Arlington, Va. Their computational analyses suggest that these genes come from bacterial consorts that live as endosymbionts within N. vectensis rather than from horizontal gene transfers or other sources. Details appeared August 30, 2013 online in Applied and Environmental Microbiology (79:6868–6873; doi: 10.1128/AEM.01635-13).

The research grew out of an unrelated project of sequence analysis of the global bacteriophage gene repertoire, according to Artamonova. “Arcady was comparing genes from different bacteriophages to sequence databases.”
she says. “He found that some phage-specific gene products were similar to other phages, and also to *N. vectensis* sequences, though not to any other eukaryotic proteins. This did not make sense, and so he suggested that we study these similarities further.”

Bioinformatics analysis suggests that the oddball genes belong to bacterial consorts of *N. vectensis*, Artamonova continues. The proteins that these genes encode group closely with bacterial or bacteriophage proteins on phylogenetic trees. Moreover, these genes lack introns, and any of their seeming intron features prove to be false clues, she adds. Finally, these bacterial-like genes are located on separate DNA fragments, all of which lack eukaryotic genes and have nucleotide compositions that are distinct from those of eukaryotic genes.

On this basis, “most of the bacterial-like genes identified in the *N. vectensis* genome are not from *N. vectensis*, but from the bacterial consorts of the starlet sea anemone,” Artamonova and Mushegian say. “Based on the analysis of protein homology of the bacterial-like proteins, we propose that these novel, uncharacterized bacteria associated with *N. vectensis* are a proteobacterium and a bacteroidetes.”

This new evidence fits with studies of *N. vectensis* from 2008 and of another cnidarian, *Hydra magnipapillata* in 2010—in both cases, consistent with these species supporting endosymbiotic relationships with bacteria, according to Artamonova. “We expect that now anatomists will look for the bacteria living inside *N. vectensis*, and microbiologists will be trying to isolate these bacteria,” she says.

The formerly iconoclastic idea that organisms exchange genes throughout their evolutionary development is now widely accepted, Artamonova continues. This new work “provides a cautionary note to the attempts to explain the presence of phylogenetically unusual genes in a genome by horizontal gene transfer,” she and her collaborators point out. “In some situations, the presence of microbial genes in a draft eukaryotic genome may tell us about real bacteria closely associated with the host.”

Thomas C. G. Bosch of the University of Kiel, Germany, agrees with Artamonova and Mushegian in this assessment. “The finding of bona fide microbial genes in a *Nematostella* genome underlines that any organism, including humans, should be considered a holobiont or metaorganism, consisting of a multicellular host and a community of associated microorganisms, which influence fitness and, thus, ecologically important traits of their host,” he says.

David C. Holzman is the Microbe Journal Highlights Editor.

**RESEARCH ADVANCES**

**Enveloped Viruses Bind Receptors on Immune Cells, Blocking Their Response**

Carol Potera

Through phosphatidylserine residues on their outer lipid membranes, several enveloped viruses bind specifically to Tyro3/Axl/Mer (TAM) kinase receptors on cells of the immune system, turning off type I interferon signaling and making the host more susceptible to these viruses, according to Greg Lemke at the Salk Institute for Biological Studies in La Jolla, Calif., and his collaborators. This point of host vulnerability, however, can be turned to an advantage, they report. Specifically, inhibitors of TAM kinases can prevent viruses from binding and activating these receptors. Details appear August 14, 2013, in *Cell Host & Microbe* (doi: 10.1016/j.chom.2013.07.005).

Lemke and his collaborators grew viruses in bone marrow-derived dendritic cells from mice, with some cells intact, others lacking either Tyro3, Axl, or Mer, and with still others lacking all three TAM receptors. Any of those cells, particularly those lacking all three TAM receptors, are less susceptible...
than wild-type cells to infections by enveloped viruses, including Ebola, West Nile, and murine leukemia, according to Lemke. Moreover, treating the triple knockout cells with an antibody that neutralizes type I interferon restores viral replication to levels seen in wild type cells.

In healthy mammalian tissues, dendritic cells of the immune system that bear phosphatidylserine and TAM receptors clear apoptotic cells through phagocytosis. Like apoptotic cells, enveloped viruses dock on the same receptors to enter—and infect—such cells. “In doing so, the virus shuts down the immune response in dendritic cells, which otherwise would mount a strong interferon response,” Lemke says.

After uncovering the TAM receptor process, Lemke and his collaborators tested BMS-777607, an orally administered kinase inhibitor that was developed to treat solid tumors and is used in cellular and animal studies. When administered in vitro, BMS-777607 markedly reduces WNV infections 10-fold in dendritic cells. Low-molecular-weight kinase inhibitors are a potentially attractive treatment option for blocking enveloped viruses, according to Lemke. “There’s an extensive pipeline of these compounds that are designed for other indications like cancer,” he says. “We can test them right away without developing our own.”

“By engaging TAM receptors, enveloped viruses may be able to convert interferon from a sworn enemy to an ally,” says Sonja Best, chief of the Innate Immunity and Pathogenesis Unit at Rocky Mountain Laboratories in Hamilton, Montana, who was not involved in the study. “In so doing, antiviral responses are suppressed just as replication gets underway—an impressive feat for a virus that is playing dead.” Kinase inhibitors that target host receptors like TAM “represent tangible clinical opportunities for the treatment of acute viral infections,” she adds.

Identifying drugs effective against the dengue fever virus, which each year infects as many as 100 million people worldwide, would be a welcome development, according to Lemke. Despite efforts to develop vaccines to prevent such infections, the latest versions have failed, he says. “A TAM inhibitor may help treat dengue until an effective vaccine becomes available.”

Carol Potera is a freelance writer in Great Falls, Mont.

RESEARCH ADVANCES

In Ocean Sediments, Phages Outnumber Hosts, Raising Questions

Barry E. DiGregorio

Bacteriophages outnumber bacterial cells in deep and ancient oligotrophic subsurface ocean sediments, according to paleomicrobiologist Bert Engelen of the University Oldenburg in Germany and his collaborators. These numbers suggest that phages are a major controlling factor for cell abundance, diversity, and life in the deep marine biosphere, they say. They presented their findings during the 2013 Goldschmidt Conference, held last August in Florence, Italy.

Bacterial cell numbers from core sediments indicate that the marine subsea floor is one of the largest reservoirs of biomass on Earth. However, low energy and nutrient fluxes along with geochemical pore water profiles suggest that the metabolic activities of subsurface microorganisms are extremely low.

Engelen and his colleagues began studying phages in subsurface sediments in 2008. At that time, little or no data were available to assess the viral impact on local microbial communities and related carbon cycling in the

MINITOPIC

Microbes, Infectious Agents on the Brain: Recent Developments

Noteworthy recent developments involving the brain and infectious agents include:

- A recombinant version of the human prion protein, which was generated in Escherichia coli cells and thus stripped of carbohydrates, can stop the propagation of prions, according to Wen-Quan Zou of Case Western Reserve School of Medicine in Cleveland, Ohio, and his collaborators. Details appear October 9, 2013 in Scientific Reports (doi:10.1038/srep02911).
- The non-protein amino acid β-N-methylamino-L-alanine (BMAA), which some kinds of cyanobacteria produce, can be “misincorporated” into neuroproteins—including in the brain tissues of patients with amyotrophic lateral sclerosis—causing them to misfold and aggregate, according to Rachael Anne Dunlop of the University of Technology in Sydney, Australia, Paul Alan Cox of the Institute for Ethnomedicine in Jackson Hole, Wyo., and their collaborators. Details appear September 25, 2013 in PLoS ONE 8(9): e75376. (doi:10.1371/journal.pone.0075376).
- The mosquito-borne eastern equine encephalitis was responsible for an outbreak among humans in Panama in 2010, marking the first time this virus moved from horses into humans in Latin America, according to Scott Weaver of the University of Texas Medical Branch, Galveston, and his collaborators. Details appear in the August 22, 2013 New England Journal of Medicine (doi: 10.1056/NEJMoA1212628)
marine deep biosphere. “We assumed that in this nutrient-limited environment, phages might play an important role,” he says. “The first step was to induce prophages from our deep-subseafloor bacteria that were already present in our culture collection.” Based on sequencing data from collaborators at the Broad Institute in Cambridge, Mass., he continues, “we were able to describe the biogeography of *Rhizobium radiobacter* and the distribution of associated temperate phages in deep subseafloor sediments. This investigation already gave a first hint for high numbers of phages within the marine subsurface.”

To verify those findings, Engelen and his collaborators directly counted phage particles within a comprehensive set of globally distributed subsurface sediments. “It turned out that phages always outnumbered the prokaryotic cells, which was known from the water column but never shown for sediments,” he says. “We want to know if viral lysis can provide essential nutrients for deep subsurface populations.

“The virus-to-cell ratios increase dramatically with decreasing substrate availability,” he continues. “What surprised us the most was the fact that the amount of phage-bound organic carbon reaches high percentages or even seems to exceed the microbial biomass in deeper and more oligotrophic sediment layers.”

“These are very intriguing results,” says John Baross of the University of Washington, Seattle, who suggests that, if anything, the phage estimates might be on the low side. Several findings “are not well understood,” he adds, pointing to questions about how these phage manage to contact hosts that are in such low abundance and the possibility that these phages might be very old. “These investigators have done some interesting work indicating a high incidence of lysogenic bacteria in sediments, opening up the possibility that the incidence of lysogeny increases with depth in the sediments,” he continues. “Cool stuff—but with puzzling phenotypic consequences. It is possible that many of these phages were induced while the sediment core was brought to the surface and during extraction.”

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**NEW IN ASM JOURNALS**

**CRISPRs: Continuing Promise for Identifying, Containing Disease Outbreaks**

Rapid, accurate strain identification is critical to timely diagnosis and treatment during outbreaks of microbial diseases. Clustered regular interspaced short palindromic repeats (CRISPRs) are one of several recently developed approaches to subtyping. Now, in a review, Nikki Shariat and Edward G. Dudley of the Pennsylvania State University, University Park, provide a historical perspective on CRISPRs and describe advances in their use for subtyping, which Shariat says is critical to containing disease outbreaks. CRISPRs are particularly useful for typing because these sequences, which can be characterized as spacers between each repeat, “are unique and are gained from other DNA entities such as bacteriophages and plasmids,” says Shariat. “When closely related bacterial strains contain varied patterns of spacers, we can sequence these DNA regions to identify the different bacterial strains,” she says. CRISPR typing is also faster and less expensive than other methods, and enables easy data sharing among laboratories.

CRISPR-based typing techniques have been well-established for some bacterial species, such as *Mycobacterium tuberculosis*, and in numerous others, including human pathogens such as *Salmonella enterica*. In species important to agriculture, such as *Erwinia*, they are currently being developed and tested and databases are being populated. Shariat notes that nearly half of all bacterial genomes contain CRISPRs. That promises that this approach may be broadly applicable both to pathogenic bacteria and to tracking specific commercialized bacterial strains. Shariat and Dudley suggest that CRISPR-based sequence typing will remain important even as whole genome sequencing becomes increasingly inexpensive, because CRISPRs “will be routinely extracted from draft genomes using automated bioinformatics tools,” along with other genetic targets such as virulence genes. Resources are available, including “friendly, free access tools,” they add, noting the CRISPRs Web server (http://crispr.u-psud.fr).


**NEW IN ASM JOURNALS**

**Probiotics Reduce Pathogens in Livestock Gut, May Substitute for Antibiotics in Feed**

For decades, now, copious antibiotics have been added to livestock feed to promote growth, which they probably do by reducing infectious disease among the animals that are often kept in severely crowded conditions. New research by Carmen Bednorz of the Freie Universitat Berlin and collaborators, conducted in the wake of the European Union’s 2006 ban on antibiotics in animal feed, suggests that feeding probiotics to livestock could substitute for antibiotics. In the study, in piglets, “We found a clear reduction of *Escherichia coli* strains possessing typical genes for extra-intestinal pathogenic
E. coli (ExPEC),” says Bednorz. The reduction was particularly noticeable in strains that adhere to the intestinal mucosa, which was “very interesting,” she says, because “ExPEC typically harbor a lot of adhesion genes that promote colonization of the mucosa.”

In previous studies, the working groups from Bednorz’ institution’s Institute of Microbiology and Epizootics found feeding Enterococcus faecium-containing probiotic to swine did not change their intestinal microbiota, but reduced infections by Chlamydia spp. and by pathogenic E. coli. While a number of strains of E. coli are pathogenic, nonpathogenic E. coli “contributes to the maintenance of the microbial gut balance,” according to the report.


NEW IN ASM JOURNALS

Drug Inhibits Development of Periodontitis in Animal Models

The researchers began their search for a therapy for periodontitis by studying the symbioses of the periodontal pathogens, using genomics, proteomics, and metabolomics, in animal models of this condition. They found that the periodontal biofilm depended for growth on the availability of iron and heme (an iron-containing molecule related to hemoglobin), and that restricting these reduced levels of the enzyme, fumarate reductase. Since Oxantel was known to inhibit fumarate reductase in some bacteria, they then successfully tested its ability to inhibit fumarate reductase activity in Porphyromonas gingivalis, a major bacterial component of periodontitis biofilms. Fumarate reductase is absent from humans, making it an ideal drug target. They also showed that Oxantel disrupted the growth of polymicrobial biofilms containing P. gingivalis, Tannerella forsythia, and Treponema denticola, a typical composition of periodontal biofilms, despite the fact that the latter alone is unaffected by Oxantel.

The researchers found that treatment with Oxantel downregulated six P. gingivalis gene products, and up-regulated 22 gene products, all of which are part of a regulon that controls availability of heme.


NEW IN ASM JOURNALS

New Method Promises Faster Identification of Blood Pathogens, Enabling More Effective Treatment

Time is of the essence when patients present with symptoms of suspected sepsis. Doctors immediately prescribe a cocktail of broad spectrum drugs to help clear the infection, based on clinical symptoms, patient demographics, and clinical guidelines or antimicrobial stewardship programs. But despite the best intentions, empirical therapy is not universally effective, and delays in appropriate therapy result in increased mortality. Conversely, sometimes that therapy is unnecessary. Faster identification of pathogens leading to more targeted treatment results in better outcomes, and less reliance on broad-spectrum antibiotics can reduce resistance.

Now John D. Walsh and colleagues of bioMérieux, Durham, N.C., have developed a new laboratory technique that combines a simple sample preparation step with rapid optical technology to identify microorganisms directly from a positive blood culture. “We see the real benefit of this new technique in its potential to be integrated into the next generation of automated blood culture systems,” says Walsh. “The inherent simplicity, safety, and low cost of the method enable it to be embedded into an instrument that will automatically receive a positive blood culture bottle from a companion detection instrument, process a sample, and deliver an electronic ID, all within a few minutes after detecting growth.” Robotics and liquid handling will enable automation of screening tests for major resistance markers and other applications, he says. Once an identification is made, positive bottles can be forwarded to the main microbiology laboratory for definitive antimicrobial susceptibility testing.