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 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.

Jeffrey L. Fox is the Microbe Current Topics and Features Editor.

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 Ghannoum of Case Western Reserve University in Cleveland, Ohio, and Chairman of the Oral HIV AIDS Research Alliance (OHARA), who spoke during

MINITOPIC
2013 Nobel in Medicine: Studies of Transport in Yeast and Mammalian Cells

The 2013 Nobel Prize in Physiology or Medicine recognizes three scientists for their work on cellular transport systems—Randy Schekman of the University of California, Berkeley, James Rothman of Yale University in New Haven, Conn., and Thomas Südhof of Stanford University in Stanford, Calif. Although all three of them studied transport of materials within living cells, Schekman during the 1970s chose to look at cell transport in the yeast Saccharomyces cerevisiae, taking advantage of its genetics to study cell physiology and biochemistry. For example, he used a genetic screen to identify yeast cells with defective transport, in which vesicles piled up in some parts of those cells. He then identified three classes of genes that control different facets of this internal transport system, including blocks in traffic from the endoplasmic reticulum, the Golgi complex, and to the cell surface. He also determined the sequence of posttranslational events affecting how these cells export glycoproteins. Meanwhile, Südhof focused his attentions on neurotransmitters, while Rothman studied how vesicles dock and fuse with membranes in mammalian cells.
CURRENT TOPICS

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