Chair's Letter

Happy Spring SOID members! I hope everyone enjoyed the relatively warm winter and are looking forward to a sunny spring. It is hard to believe that summer is just around the corner. Our training fellow liaisons have been busy working on different initiatives for the section. In the fall, the SOID was invited by the European Pediatric Society to contribute an article to their newsletter. Dr. Rana Hamdy, a third year pediatric infectious diseases fellow at Children’s Hospital of Philadelphia, Dr. Zachary Willis, a third-year fellow at Vanderbilt University Medical Center and SOID member Dr. Michael Klatte, wrote an outstanding article on “Addressing antibiotic resistance with stewardship”, which was very well received. And in this edition of the SOID newsletter, our fellows Dr. Ishminder Kaur, a second year fellow at St. Christopher's Hospital in Philadelphia and Dr. Rana Hamdy have written a very concise article addressing the practical use of “Rapid diagnostic tests in infectious diseases” which I encourage you to take a look at.

Thank you to SOID members, Dr. Charles Woods and Dr. Mayssa Abuali, who have served on the Education Subcommittee for the past several years. Dr. Woods is currently serving as the liaison between the SOID and the Pediatric Infectious Diseases Society (PIDS). Welcome to new Education Subcommittee members:

- J. Michael Klatte, MD, FAAP
- Grace Lee, MD, MSCE, FAAP
- Angela L. Myers MD, MPH, FAAP
- Kari Simonsen, MD, FAAP

One of the major goals of the SOID is to strengthen our relationship with PIDS in order to expand the educational and

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Chair's Letter

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networking venues available to our membership. We also work collaboratively with the COID (Red Book Committee) on a variety of projects. The SOID is currently working with PIDS and members of the COID on an antibiotic resistance and antibiotic stewardship initiative, the first meeting of which was held in October at the 2015 AAP National Conference and Exhibition (NCE) meeting. The objectives of this workgroup are to develop resources and strategies centered on education, clinical guidance, policy and research in the area of pediatric antibiotic stewardship and antibiotic resistance for both the inpatient and outpatient settings. The SOID is actively working on developing a section program on antibiotic stewardship in the office setting for the 2017 NCE meeting. We also continue to work with other AAP sections to develop joint educational programs for the NCE. This is a very important way to provide infectious diseases education on a variety of topics to a broad group of both general and subspecialty healthcare providers.

I am excited to announce that the inaugural S. Michael Marcy visiting professorship will take place at the University of South Dakota Pediatric Residency Program - Sanford School of Medicine in June 2016. Dr. Meg Fisher will serve as the visiting professor for this program. I would like to congratulate both parties on this honor. As a reminder, this program has been designed to bring nationally and internationally known pediatric infectious diseases specialists to pediatric and family practice programs around the country that may not have or who have limited access to a pediatric infectious diseases specialist. The professorship would give these programs an educational opportunity to have the visiting professor address infectious diseases issues that the program may be dealing with and allows for ample interaction between the visiting professor and members of the program and community physicians in which the program is located. The program has been very well accepted since it launched and there have been a number of applications submitted by various institutions for the next cycle. These applications will be reviewed by the SOID Executive Committee over the next several months and the selected institution will be notified and announced.

Zika virus, which is primarily transmitted by the *Aedes aegypti* mosquito, is found throughout much of Central and South America, southern parts of the United States and in the Caribbean, has been prominently in the news due to evidence suggesting an association of Zika virus infection with an increased risk for congenital microcephaly and other abnormalities of the brain and eye. Because of multiple outbreaks of the disease and the significantly increased number of infants born with microcephaly and other anomalies (especially in Brazil), on Feb 1, 2016, the World Health Organization declared the Zika virus outbreaks a Public Health Emergency of International Concern. The CDC has come out with guidelines for the healthcare provider on the care of pregnant women and women of reproductive age with possible Zika virus exposure (Oduyebo T, et al. *MMWR* 2016; February 12;65(05):122–127), on the evaluation and testing of infants with possible congenital Zika virus infection (Staples et al. *MMWR* 2016 February 26;65(7);182–187) and on the care of infants and children with possible Zika virus infection (Fleming-Dutra et al. *MMWR* 2016 January 29;65(3):63-67). More recently, an article was published in *Pediatrics* from the CDC, “Zika Virus Disease: A CDC Update for Pediatric Health Care Providers” (http://pediatrics.aappublications.org/content/early/2016/03/22/peds.2016-0621). In this edition of the newsletter, there are two comprehensive articles on Zika virus that I encourage you to check out.

Vaccination rates for human papillomavirus (HPV) vaccine in both teenage females and males remain well below the rates for other routine vaccines with only slight increases compared to last year. Data from the 2014 Center for Diseases Control and Prevention's (CDC) National Immunization Survey showed that overall rates of completion for the three dose series among US adolescent females and males between the ages of 13 and 17 years was 39.7% and 21.6% respectively. This is somewhat disappointing given that multiple studies have shown that this vaccine is having a significant impact on decreasing the incidence of genital warts and anogenital cancers. Also a recent article published in *Pediatrics* (Markowitz LE et al. *Pediatrics* 2016;137(2):e20151968) demonstrated that within 6 years of HPV vaccine introduction, there was a 64% decrease in HPV4 vaccine serotype prevalence among females aged 14 to 19 years and a 34% decrease among those aged 20 to 24 years. These findings further emphasize the effectiveness of HPV vaccine and demonstrates the first national evidence of impact among females in their 20s. Because of the persistently low HPV vaccination rates, the CDC, AAP and other organizations continue to develop strategies to try and increase these rates. Multiple members of the AAP SOID and COID have been working with the AAP to develop programs that are aimed at improving awareness and education of both healthcare providers and the public on the importance of administering HPV vaccines to the teenage population. The HPV Champion Toolkit has been developed to provide practices with easy access to the best resources available regarding HPV vaccination.
Finally, whether you are a general pediatrician with a specific interest in infectious diseases or a pediatric infectious diseases subspecialist, I encourage you to take advantage of the many educational opportunities in which the SOID is involved. Whether it is specific infectious diseases programs at the NCE (2016 NCE in San Francisco, CA), attendance at the various different PREP Board Review Courses, or through the AAP SOID Website with new Pedialink courses, the SOID is strongly focused on the education of our members. New programs are in the works, so please stay tuned. I would also like to encourage members who are interested in serving the SOID on educational issues or who have suggestions for educational topics, website issues or the newsletter subcommittees to please contact us or complete the 8-question expertise and interest survey.

I very much look forward to receiving your ideas and suggestions as we go forth and thank you for your continuing interest and membership in the SOID. Please don't hesitate to contact Suzanne Kirkwood, the SOID manager and staff liaison at the AAP (SKirkwood@aap.org) or myself (ttan@northwestern.edu or titan@luriechildrens.org) to let us know how we can best serve your needs.

Best wishes for a great spring and summer.

Tina Q. Tan, M.D., FAAP, FPIDS, FIDSA

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**PREP ID Self-Assessment**

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From Aedes to Zika: Mosquito-Borne Diseases in the U.S.

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Co-Chairs of the Infectious Disease Committee of AAP District II, Chapter 2

One-third of the world’s population is at risk for dengue virus (DENV) infection, with 390 million infections occurring annually from the bite of an infected female Aedes aegypti or Aedes albopictus mosquito. Fortunately, up to 75% of infections are asymptomatic. Dengue is endemic in the US Virgin Islands, American Samoa, and Puerto Rico, where 3000-9000 suspected cases occur annually in nonepidemic years. Most U.S. cases result from travel to an endemic area, but locally-acquired dengue has been documented in Texas, South Florida, and Hawaii. Both Aedes species are found in the U.S.

Classic dengue fever presents as a flu-like illness, “break-bone fever”, after 4-7 days incubation, but occurs in < 60% of patients. Children often have milder symptoms. The critical dengue disease occurs in about 1% of patients, usually children and young adults, as they defervesce after 3-7 days. Systemic vascular leakage lasting 48-72 hours can result in life-threatening dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS). Children with DHF rarely have clinically-significant bleeding, but adults often exhibit hemorrhaging in the skin and gastrointestinal tract. DSS patients appear well, but once they become hypotensive, irreversible shock and death can occur despite aggressive resuscitation. Signs of impending shock include persistent vomiting, increasingly severe abdominal pain, tender hepatomegaly, mucosal bleeding, lethargy or restlessness.

Infection with and immunity to one DENV serotype may predispose individuals to DHS or DSS from another of the four serotypes that infect humans, so most travelers, except for those frequently visiting family and relatives (VFR), are unlikely to develop severe dengue. Dengue management is supportive. Careful, frequent assessment of heart rate, blood pressure, high or rising hematocrit, and urine output with administration of fluids, including oral, intravenous, and blood products to maintain adequate intravascular volume, is critical to recognize impending shock. There is no currently effective antiviral for DENV, but a recombinant live attenuated tetravalent vaccine (CYD-TDV) may be approved in 2016.

Chikungunya virus (CHIKV) is spread by the same mosquitoes as DENV. In contrast to DENV, 85% of CHIKV infections are symptomatic. Recent CHIKV outbreaks have been associated with widespread epidemics with high attack rates in South Asia, Europe, the Caribbean and the Americas. At least 11 endemic cases have been documented in the U.S. After a brief incubation of 2-4 days, patients experience rapid onset of fever to 39-40°C, followed by a symmetric polyarthritis in 2-5 days, more common in distal large joints. Patients are often immobilized by pain. A macular or maculopapular rash beginning on the trunk or extremities is also common after three or more days, and lasts three to seven days. The rash can be patchy or diffuse, and may be pruritic in up to half of patients. Petechiae and bruising are uncommon, but infants and vertically infected neonates may develop bullae. Gastrointestinal symptoms and erythematous ears from CHIKV chondritis occur as well.

Zika virus (ZIKV) was originally isolated by scientists studying yellow fever in the Zika forest of Uganda in 1947, with only 14 confirmed human cases in Africa and Asia for 60 years. In April 2007, an outbreak occurred in Micronesia, followed by further epidemics in Oceania, including French Polynesia where over 30,000 estimated cases occurred between October 2013 and March 2014. An outbreak began in Brazil in April 2015 and has spread throughout the Americas, including the Caribbean, and remains ongoing as of March 2016. The primary vector appears to be Aedes mosquitoes, although ZIKV has been detected in other mosquito species, such as Anopheles and Culex. As of March 16, 2016, there have 258 confirmed ZIKV infections in the fifty United States, all acquired through travel. However, in Puerto Rico, the US Virgin Islands, and American Samoa, 283 locally-acquired cases have been documented.

Most patients with ZIKV have symptoms similar to dengue and Chikungunya with fever, pruritic maculopapular rash, arthralgia and non-purulent conjunctivitis, which are mild and resolve within about a week. The incubation is not known but believed to be less than two weeks. There is strong evidence for a causal link between ZIKV infection and Guillain-Barré syndrome. ZIKV is the first arthropod-borne virus to be proven to be sexually transmitted via semen, where it has

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been isolated at least two weeks after infection. There is also a strongly suspected, but not yet scientifically proven, link between a pregnant woman being infected with ZIKV and subsequently delivering an infant with microcephaly. ZIKV has been detected in the amniotic fluid of pregnant women and in the tissue from microcephalic newborns. Research is still ongoing regarding the transmissibility and virulence of ZIKV, and the incidence of maternal-fetal transmission by trimester and risk-modifying factors.

Diagnosis of these infections is largely clinical, based on a symptomatic febrile illness with compatible symptoms, after travel to an endemic area. However, the symptoms overlap with diseases caused by other pathogens like *Leptospira*, *Plasmodium*, *Rickettsia*, parvovirus B19, *S. pyogenes*, rubella virus, measles virus, enterovirus, and adenovirus. Laboratory testing can help confirm a DENV, CHIKV, or ZIKV infection via RT-PCR if symptoms began less than seven days earlier. RT-PCR is recommended over serologies in this timeframe, since DENV and ZIKV are both flaviviruses, with cross-reactivity between their IgM assays. Four or more days after symptom onset, performing an IgM assay for each virus is appropriate. Positive results should be confirmed with a plaque reduction neutralization test (PRNT) against other flaviviruses, both local and from the country of travel.

Testing should be performed on all pregnant women with clinically-compatible symptomatic illness and possible recent travel or sexual exposure, and preferentially should be performed at time of clinical illness. For asymptomatic pregnant women with possible exposure, ZIKV IgM testing can be offered and performed 2-12 weeks after exposure. If negative, a fetal ultrasound to detect microcephaly or intracranial calcifications should be done. If positive, serial fetal ultrasound and an amniocentesis for ZIKV should be considered. At present, while some commercial labs can test for CHIKV and DENV, there is only one DENV test that is FDA-approved. Healthcare providers should contact their state health department to arrange for submissions of clinical samples to be tested. All of these viral diseases are reportable.

References:

Resources:
5. MMWR Zika Reports: http://www.cdc.gov/mmwr/zika_reports.html
7. CDC Chikungunya Webpage: http://www.cdc.gov/chikungunya/
Zika virus (ZIKV) is an emerging arthropod-borne virus that belongs to the genus Flavivirus, related to dengue, yellow fever, Japanese encephalitis, and West Nile viruses, and transmitted primarily by *Aedes spp.* mosquitoes. For 60 years, after it was first isolated from a rhesus monkey in a forest in Uganda in 1947, ZIKV has been only associated with sporadic cases in humans in Africa and Asia. However, since 2007 when the first outbreak of ZIKV outside Africa and Asia was reported (in the Federated States of Micronesia (Yap), it has been identified in subsequent outbreaks in Southeast Asia and the Western Pacific. In May 2015, the Ministry of Health of Brazil confirmed autochthonous transmission of ZIKV associated with an outbreak of “dengue-like syndrome” cases in north-eastern Brazil. The ZIKV outbreak continued to evolve, spreading geographically very rapidly in the Americas. As of March 3, 2016, 31 countries and territories in the region, including several United States (US) territories, identified autochthonous cases. It has been estimated that between 440,000 and 1.3 million cases of ZIKV occurred in Brazil, the most affected country, in 2015.

The infection, when symptomatic, was previously considered to be associated with a mild, self-limited disease, lasting few days and characterized by low fever, a pruritic rash, edema of extremities, headache, retro-orbital pain and myalgia. Severe presentations of the disease or deaths associated to ZIKV infection were not reported before the outbreaks in French Polynesia and Brazil. However, the results of a recent study in a large series of patients from French Polynesia who developed Guillain-Barré syndrome (GBS) following ZIKV infection, suggested that ZIKV should be included in the list of potential infectious pathogens that can trigger the development of GBS. In Brazil, hospital-based surveillance data revealed a significant increase in the number of GBS cases and other neurological and auto-immune complications reported during the recent outbreak in several states from the northeastern region. Furthermore, Colombia and Venezuela also reported an increase in the rates of GBS compared to previous years. In Colombia, preliminary reports indicated that, from epidemiological week (EW) 51 of 2015 to EW 3 of 2016, all reported GBS cases presented a clinical history compatible with a previous ZIKV infection.

The most striking finding during the ZIKV outbreak in Brazil, however, is the cumulative evidence establishing a potential link between ZIKV infection during pregnancy and fetal and placental abnormalities, including fetal death, congenital neurologic and ocular disease, intrauterine growth restriction, and placental insufficiency.

Since September 2015, in the north-eastern region in Brazil, where ZIKV outbreaks peaked, a significant increase in the number of newborns with microcephaly, compared to the median rates reported in previous years to the local health authorities, was observed. On November 12, 2015, the Ministry of Health of Brazil declared the situation a Public Health Emergency of National Importance and the health authorities started an investigation of the potential causes of the public health emergency. As of February 27, 2016, 5909 suspected cases of microcephaly and/or central nervous system malformations, including 139 deaths, were reported in Brazil—1687 of these have been investigated further and, among these cases, 641 had clinical and laboratory characteristics compatible with a congenital infection, and 82 had laboratory-confirmed ZIKV infection.

Evidence of a link between ZIKV infection in pregnancy and fetal malformations was established after the detection of virus genome by reverse transcriptase-polymerase chain reaction (RT-PCR) in amniotic fluid samples of women whose fetuses have been diagnosed with microcephaly, in placental tissues from early miscarriages and also in the blood and brain tissue of infants with congenital neurologic anomalies, including microcephaly. The neurologic malformations were characterized predominantly by microcephaly (with significant cranium-facial disproportion) and cerebral calcifications, but lissencephaly with agenesis of the corpus callosum, pachygyria, hydrocephalus and cerebellar dysplasia were also reported. The severity of the neurologic alterations appears to be related to the period of gestation when the women are infected, i.e., the earlier the infection during pregnancy, the more severe the neurologic outcomes to the fetus. Arthrogryposis, microphthalmia, funduscopic alterations in the macular region, as well as optic nerve abnormalities also were described in infants with suspected congenital ZIKV infection.
In a study performed in Rio de Janeiro, women infected during pregnancy with ZIKV were followed prospectively, and clinical and ultrasonographic data were collected. The authors found that fetal abnormalities were detected by Doppler ultrasonography in approximately 30% of the women. Also important was the finding that neurological congenital abnormalities were seen in fetuses infected as late as 27 weeks of gestation.

The true burden of the congenital disease associated with ZIKV is probably underestimated assuming that it is likely that a significant proportion of the affected newborns have subclinical manifestations at birth, without microcephaly, preventing these infants from being diagnosed by the current ascertainment methods, at least until later stages of childhood/adolescence when cognitive, developmental and/or visual limitations can be detected.

Interestingly, studies in animal models performed in the 1950s have previously demonstrated the potential neurotropism of the ZIKV.

The unique characteristics of the ZIKV outbreak in Brazil, where the population was completely susceptible (naïve) to the virus, affecting millions of persons from highly populated urban areas with established surveillance reporting systems, are possible reasons explaining why the role of the ZIKV as a potential cause of congenital disease has only been recognized after circulating in Brazil.

Although causality is not yet unequivocal, the outbreak in Brazil provided strong evidence of the potential role of the ZIKV as a cause of neurologic congenital disease. The significant increase in reports of microcephaly and other neonatal neurologic malformations during this outbreak emphasize the need to strengthen laboratory capacities and establish a quality surveillance system to detect these cases and confirm the association with ZIKV infection with well-designed epidemiological studies.

Other neighboring countries also should be alerted to the potential role of ZIKV as a cause of congenital neurologic disease, and any increase of microcephaly or other neurological congenital alterations must be evaluated and investigated.

Last, but not least, it is of paramount importance that health authorities in Brazil, as well as other countries in the region, intensify the efforts to control the *Aedes aegypti* mosquito, the same vector responsible for transmitting dengue and chikungunya. In the short-term, this is the most efficient measure to mitigate the huge public health burden of these infections.

**References:**

8. Schuler-Faccini L, Ribeiro EM, Feitosa IM, et al. Possible association between Zika virus infection and microcephaly

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Zika virus in Brazil: lessons learned . . . Continued from Page 7


AAP State Government Affairs Updates - Parental Attitudes About Vaccines: The Tide Continues to Turn

A recent Health Affairs article examined the influence of last year’s measles outbreak on parental attitudes about vaccines. The study finds that parents who were more aware of the measles outbreak were more likely to be confident in vaccine safety and efficacy, and were also more likely to support state laws requiring children to be immunized as a condition of school entry. This confirms earlier public opinion polling from CS Mott Children’s Hospital National Poll on Children’s Health and Truven Health Analytics that parental attitudes about childhood vaccines are shifting dramatically towards an increased awareness of the importance of routine childhood immunization.

State legislative actions in 2016 on state immunization exemption policies are already building on the watershed events in California and elsewhere last year in the effort to protect children from vaccine preventable diseases.

For more from the AAP on this issue, please see our Childhood Immunizations State AdvocacyFOCUS resource and our Immunization Initiatives pages. Working on this issue in your state? Contact us at stgov@aap.org.
ID Training Fellows Column: Rapid Diagnostic Tests in Infectious Diseases

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Increasing Use of Rapid Diagnostic Tests
Over the past decade, physicians expect short turn-around-times for diagnostic tests. The timeline has changed from weeks to days to hours and continues to evolve. Rapid diagnostic assays can decrease time to completion, detect pathogens for which only limited testing existed previously and even generate results that providers had not requested. In this article, we will explore the different types of rapid diagnostic tests and their respective value in clinical care.

Types of Rapid Diagnostic Tests
Rapid diagnostic tests can be categorized by (1) their technologic basis, such as nucleic acid detection via qualitative or quantitative polymerase chain reactions (PCR), fluorescence in situ hybridization, microarray, or species-specific microbial analyte detection via matrix-assisted laser desorption ionization, time-of-flight mass spectrometry (MALDI-TOF MS), electro spray ionization or whole genome sequencing; (2) the number of pathogens targeted (single vs multiple); (3) the specimen type (respiratory secretions, cerebral spinal fluid (CSF), blood, stool, urine, other bodily fluids or tissues); and d) results generated including pathogen detection, antimicrobial susceptibility, genetic drug resistance markers, molecular typing.

Multiplex PCR based-panels are used widely in clinical laboratories. These panels can detect multiple bacteria, viruses and parasites simultaneously in a single specimen without the physician suspecting or requesting testing for individual pathogens. Several FDA-cleared panels currently are available for detection of pathogens of respiratory tract, bloodstream, gastrointestinal and central nervous system (CNS) infections. Pathogen identification is limited to the manufacturer's selected nucleic acid targets, usually without the user's ability to modify targets within a panel.

MALDI-TOF MS identifies organisms by analyzing a single microbe's analytes (proteins, phospholipids, lipopeptides) produced by laser ionization and compares each organism's unique molecular mass spectrum with a database of reference organisms. The expansive pathogen identification still is limited by entries in the database, but MALDI-TOF MS has the potential to expand with addition of newer entries. MALDI-TOF MS also could be applied as a rapid testing system for antimicrobial resistance to detect the presence of cleaving enzymes, such as β-lactamases, by measuring the break down product of the antibiotic in the presence of enzyme-producing microorganisms.

Most rapid assays for bloodstream infection have required growth in blood culture media in contrast to direct testing that can be performed on diarrheal stool and respiratory tract specimens. Systems under development aim to detect pathogens directly from a positive blood culture bottle or directly from a blood specimen. For example, the FDA-cleared T2Candida test can detect Candida species directly from whole blood with possible identification to the species level within hours of a patient presenting for medical attention.

Clinical Role of Rapid Diagnostic Testing
Turnaround time for the rapid assays ranges from 20 minutes to five hours. In patients with bloodstream infections, integrating rapid diagnostic tests with antimicrobial stewardship programs can possibly favorably affect time to appropriate antimicrobial therapy as well as hospital length of stay and healthcare costs. Rapid detection of respiratory pathogens via real-time PCR (RT-PCR) of nasopharyngeal and/or oropharyngeal specimens increases diagnostic yield, especially for virus detection. However, studies to date show inconsistent effects on outcomes such as antibiotic use, cost, hospital admission and length of stay. Rapid detection of multidrug-resistant tuberculosis (MDR-TB) (via the Genotype MTBDRplus or Xpert® MTB/RIF) has been shown to reduce the time to initiation of appropriate therapy, conversion to sputum negativity and improvement of infection prevention. Rapid identification of multidrug-resistant organisms and viral respiratory pathogens also can lead to earlier implementation of hospital infection prevention practices.

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to reduce transmission and potentially avoid outbreaks of hospital-acquired infections. The high resolution power of whole genome sequencing to detect strain differences lends itself to application in outbreak investigation and studies of modes of transmission with faster turnaround times compared with traditional typing techniques such as pulse field gel electrophoresis. The implementation of whole genome sequencing as a routine diagnostic tool for rapid species identification and antimicrobial susceptibility testing is under investigation.

Pitfalls in Interpretation and Challenges of Implementation

The exquisite sensitivity of molecular diagnostic tests poses a challenge of interpreting detection of microorganisms that can be commensals when specimens are taken from non-sterile body sites. For example, *C. difficile* infection has traditionally been diagnosed by detection of toxin in the stool, whereas the currently available molecular tests for *C. difficile* identify presence of toxin genes which does not prove toxin expression or production and could represent mere colonization. Asymptomatic *C. difficile* carriage (colonization with or without toxin production) is common among children under two years of age and patients recently exposed to healthcare or antimicrobial agents. Thus, detection of *C. difficile* in the stool of such patients could lead to over-utilization of antibiotics and hospital resources for patient isolation. A prospective cohort study of hospitalized adults with suspected *C. difficile* infection examining the clinical course of disease in patients with *C. difficile* toxin gene detected by PCR but without toxin detected by enzyme immunoassay (EIA) found that outcomes among patients with stools PCR+/EIA- were similar to patients without *C. difficile* (PCR-/EIA-). A recent prospective epidemiologic study has shown a high prevalence (15%) of asymptomatic colonization with toxigenic *C. difficile* in adults, not associated with recent healthcare or antimicrobial exposure. The role of these asymptomatic carriers in hospital transmission of *C. difficile* remains unclear. Pending such clarification, one might hypothesize either that enhanced detection of *C. difficile* via PCR-based tests could lead to unnecessary and potentially harmful management or could potentially improve hospital infection prevention.

The benefit of pathogen detection remains unclear for most outpatient and non-life-threatening inpatient viral infections for which clinical and seasonal prediction is good and antiviral therapy is not a consideration. Detection of viruses by rapid assays, especially viruses with known long tails of virus shedding (e.g., bocavirus and rhinovirus), can potentially distract attention from the true cause of the patient's symptoms. Detection of multiple organisms in stool or respiratory specimens by rapid assays leaves providers with the task of assigning disease causation versus asymptomatic shedding role for each microbe detected. Additionally, the detection of virus(es) or certain bacteria with prolonged shedding (e.g., *Mycoplasma pneumoniae*) in a febrile child does not exclude the possibility of a concurrent bacterial infection. The identification of newer viruses in stool specimens via next generation sequencing expands detection remarkably but poses the problem of ascribing pathogenic roles in gastroenteritis.

In addition to challenges related to cost (upfront cost of equipment, ongoing test/reagent costs, laboratory personnel training), laboratories undergoing transition to rapid tests must choose whether rapid diagnostic tests should supplement or replace routine culture techniques. With the currently limited ability of rapid assays to generate antimicrobial susceptibility results, culture still is imperative for bacteria unless antibiotic susceptibility is predictable, such as for *Streptococcus pyogenes* and *Bordetella pertussis*. Additionally, as microorganisms continue to mutate under selective pressures, or emerge, a surveillance culture system will be critical to keep up with optimal detection and optimal guidance for anti-infective therapy. Finally, with no current guidance from expert committees regarding implementation of these tests, organizations have tended to develop and implement individualized algorithms that might not always be scientifically sound.

Future Directions

Clinical studies of validation and applicability as well as education for providers must keep pace with rapidly evolving technologies of detection in order to optimally care for patients, practice antimicrobial stewardship and hospital infection prevention, and perform outbreak investigations.

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References:

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Learn how to Prevent and Treat Pertussis with NEW Online Course

Pertussis is a major public health problem in all age groups throughout the United States. Oftentimes the disease is not diagnosed, allowing it to spread. The Challenging Cases: Pertussis course will help you recognize risk factors and symptoms, identify treatment options and help prevent pertussis. Areas addressed:

- Changing epidemiology of pertussis disease
- Impact of increasing adolescent and adult pertussis illness on the community
- Cocooning strategy and other immunization strategies
- Preventative vaccines and recommended vaccination schedule
- Examination of atypical cases
- Pertussis post-exposure prophylaxis (PEP)

Qualifies for AMA PRA Category 1 Credit(s)TM. You may also be interested in the Challenging Cases: Clostridium Difficile.
**Review of the Recent Infectious Disease Literature**

These summaries and commentaries are completed by volunteer Contributing Editors from the SOID. Each is responsible for reviewing the current infectious disease literature for several journals. They select an interesting article and present it for your review to help keep you current on various issues.


Reviewed by: Sherman J. Alter, MD. Division of infectious Disease, Dayton Children's Hospital, Department of Pediatrics, Wright State University Boonshoft School of Medicine, Dayton, OH.

Infection with *Chlamydia trachomatis* is the most frequently reported sexually transmitted bacterial infection in the United States. Data from the 2007-2012 National Health and Nutrition Examination Survey (NHANES) indicate that an estimated 1.8 million persons aged 14-39 years in the US have a genital chlamydial infection.\(^1\) Reported numbers likely underestimate the disease burden because most chlamydial infections are asymptomatic and remain undetected. Untreated infections can result in ascending infections in women causing pelvic inflammatory disease which can lead to infertility and ectopic pregnancy. In men, sequelae include urethritis, epididymitis, and proctitis. Annual chlamydial screening tests are recommended for all sexually active women <25 years of age. Prompt treatment of persons infected with *C. trachomatis* with effective therapeutic agents can prevent adverse reproductive health complications and continued sexual transmission.\(^2\)

This non-inferiority study was designed to test the null hypothesis that azithromycin (AZ) treatment failure would be at least 5% higher than the rate of doxycycline (DC) failure against the alternative hypothesis that there would be no difference between regimens, with a failure rate of 3%. It was an open-label, 1:1 randomized trial of treatment (directly observed AZ 1 g single-dose or DC 100 mg twice daily for seven days) among infected males and females 12 to 21 years in four long-term, sex-segregated correctional facilities in Los Angeles. At intake, participants were interviewed and examined, and each submitted a first-catch urine specimen for nucleic acid amplification testing to screen for chlamydia. Repeat urine screens were performed at days 28 and 67 among those with intake-positive *Chlamydia* screens. Urine screens positive at first or second follow-up had OmpA genotyping performed to assess for concordant strains. The primary endpoint was treatment failure at 28 days post-treatment.

Of those infected, 284 were assigned to receive AZ and 283 to receive DC. After early discontinuation (mostly due to discharge from the facility), a total of 155 in each treatment group (65% male) made up the per-protocol population. No treatment failures occurred in the DC group (0%; 95% CI: 0.0 - 2.4). In the AZ group, seven participants (six male, one female) were *Chlamydia*-positive at first follow-up. Five of the seven were deemed treatment failures in that two participants were infected with discordant strains (3.2%; 95% CI: 0.4 - 7.4). The observed difference in failure rates between the AZ and DC groups was 3.2%, with an upper boundary of the 95% CI of 5.9%, which exceeded the 5% cut-off for establishing non-inferiority of AZ. While the efficacy of DC was 100% and AZ 97%, the non-inferiority of AZ was not established in this trial.

**Reviewer's Commentary:**
AZ therapy for chlamydial infection has been recommended for many years. Some studies have shown a lower efficacy for AZ than for DC. Obviously, single-dose AZ addresses potential nonadherence with a 7-day course of DC. While demonstrating that both agents have high efficacy rates in treating genital chlamydial infections, the authors conclude that the non-inferiority of AZ to DC could not be established. This study examined a unique adolescent population in a specific geographic location where multiple-dose DC adherence was monitored – differing from more limited adherence rates seen in the general population. Furthermore, as noted in a commentary published in the same issue of the Journal, the study used a one-sided significance level of 0.10 with 90% power, rather than the standard level of 0.05, which might have affected the sample size and potentially the outcome.\(^3\) An additional 130 participants who could be evaluated per treatment group would have been required to attain this level and increase the precision. Finally, one or two more treatment failures in the DC group, or one or two fewer failures in the AZ group, might have altered the conclusion. In the end, however, given the excellent efficacy (97% and 100%) for both antibiotics, therapy with either DC or AZ seems appropriate.

Continued on Page 13
References:


Reviewed by: Stephen C. Aronoff, MD FAAP, Temple University School of Medicine.

The goal of this study was to determine the role of vesicoureteral reflux and other factors on the rates of recurrent urinary tract infections (UTIs) and renal scarring in children. The authors identified two prospectively-followed cohorts of subjects: the placebo cohort from the Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) study (NEJM 2014; 371:1072) and a cohort of patients screened for the RIVUR study without reflux (Careful Urinary Tract Infection Evaluation; CUTIE). All subjects had a documented UTI at the time of entry into the study and underwent ultrasonography, voiding cystoureterography and DMSA renal scanning at enrollment. Subsequent scans were performed at one year (RIVUR subjects only) and two years (both groups) follow-up visits. Endpoints for the study were recurrent UTIs and renal scarring.

305 children (RIVUR) with and 195 children without vesicoureteral reflux (VUR) were included. Children without VUR were more likely to be older, African-American, publically-insured, toilet-trained and to have an afebrile UTI as the initial event compared to those with reflux. Those without VUR were less likely to have scarring at baseline. The 2-year UTI recurrence rate was higher in children with VUR than in those without (25.4% vs 17.3%. HR 1.58; 95%CI: 1.04 – 2.420); those with grade III or IV reflux had the highest rates. Non-parametric analysis demonstrated that the highest rates of recurrence occurred in children with VUR and bladder/bowel dysfunction (BBD) (56%), BBD alone (35%) and children with low grade VUR (29%). Children with and without VUR had low rates of renal scarring at baseline (3% and 2%, respectively); at 2-year follow-up children with VUR had higher rates of new scarring (10.2% vs 5.6%) and had more severe scarring (2.6% vs 0%) than children without. VUR and BBD are significant risk factors for recurrent UTIs.

**Reviewer's Commentary:**
The present study demonstrates that children with VUR and particularly those with BBD are at increased risk for recurrent UTI and that VUR alone places children at increased risk for renal scarring. Unfortunately, the long awaited RIVUR study, published in 2014, demonstrated that antimicrobial prophylaxis in children with VUR reduced the risk of UTI recurrence but not the risk of renal scarring. Moreover, prophylaxis virtually guaranteed that recurrent infections would be caused by drug-resistant organisms. So where does that leave things? It is clear that VUR increases the risk for renal scarring, a process that is unimpeded by antimicrobial prophylaxis. The observation that antimicrobial prophylaxis reduces the risk of recurrent UTI in this population argues against a causal relationship between recurrence and renal scarring in healthy children. While it is unclear what risk recurrent UTIs pose to otherwise healthy children, the risk of reinfection with drug resistant bacteria is a clear risk of antimicrobial prophylaxis. The present study identifies BBD as a factor for UTI recurrence in children with or without VUR. Given the uncertain role of antimicrobial prophylaxis, future studies should focus on the treatment of BBD and its effect on both UTI recurrence and renal scarring.


The study by Gadad et al has added to the large body of evidence refuting a causal link between ethyl mercury in the form of the vaccine preservative thimerosal and/or receipt of MMR vaccines and autism spectrum disorder (ASD). Study investigators administered thimerosal-containing vaccines according to the recommended pediatric vaccine schedules from the 1990s (which had the highest thimerosal exposure) and from 2008 (which had the greatest number of different vaccines) to infant rhesus macaques. They followed the macaques for 18 months and examined behaviors, both social and nonsocial (as an indicator for cortical function), as well as euthanized animals for neuropathology studies from three specific brain regions previously found to be affected in post-mortem ASD brains; namely a change in neuronal size in the limbic system, decreased number of Purkinje cells in the cerebellum, cortical dysgenesis or migration disturbances and changes in GABAergic and cholinergic systems in brainstem, neocortex, amygdala and hippocampus and compared these to control animals who received saline placebos. Behavior was tested using well-established, detailed protocols by three examiners who passed periodic reliability training and who were blinded to the experimental conditions of the animals. Neuropathologic measurements were conducted by at least two different investigators who were likewise blinded to the experimental conditions of the animals. The investigators found no significant differences in negative behaviors between animals in the control or experimental groups, nor did they find any cellular or protein changes in the cerebellum, hippocampus (including no effect on neurogenesis) or amygdala following the 1990s or the 2008 vaccine schedules.

Reviewer's commentary:
These results should put to rest any concerns that thimerosal or the number and timing of vaccines causes ASD. This evidence should be reassuring to pediatricians who must often attempt to convince vaccine-hesitant parents to vaccinate their children. Unfortunately, as Dr. Offit highlights in his Commentary, this might not be the case. A 2015 Medscape survey study of pediatricians revealed that the majority of parents who chose to delay, withhold, separate or otherwise alter the spacing and timing of vaccines stated the fear of autism as their reason for doing so, in spite of overwhelming evidence from both clinical and preclinical studies that discredit any potential link between vaccines and ASD. Dr. Offit rightly points out that, until science can answer what really causes ASD, many fearful parents will continue to ignore all of the scientific evidence and maintain their belief that vaccines are the cause.


Pan et al examined three Mycobacterium tuberculosis-specific bacterial small molecules (BSMs) in a proof of principle study: two mycobactin siderophores (used by the organism to bind host iron) and tuberculosinyladenosine (used by organism to prevent maturation of host derived phagosomes), both of which are intracellular survival mechanisms of M. tuberculosis. Using both mouse and human models along with liquid chromatography-tandem mass spectrometry, the investigators were able to detect the presence of one or both mycobactins and/or tuberculosinyladenosine in serum and lung tissue from infected mice as well as sputum (90%), cerebrospinal fluid (71%) or lymph nodes (40%) from infected humans, but not from uninfected controls. In addition, they were able to rapidly detect one or more BSMs in paucibacillary forms of tuberculosis (TB) comparing favorably to PCR-based detection methods. Additionally, they were able to demonstrate that BSMs correlated with bacterial load using sputum AFB smear positivity scores, mycobacterial growth indicator tube (MGIT) time-to-positivity and GeneX-pert grade for each sputum specimen examined. The investigators acknowledged the potential lack of availability of liquid chromatography-tandem mass spectrometry in most institutions, but stress that species-specific BSMs could be used in an enzyme linked immunoassay platform if
Review of the Recent Infectious Disease Literature  

Continued from Page 14

Specific antibodies could be developed, thereby creating rapid assays that would be amenable to point of care testing. If such point of care assays could be developed for the detection of *M. tuberculosis* BSMs, this would represent a valuable addition to our existing TB diagnostic tools and might greatly help with the diagnosis of TB disease in children.

**Reviewer's Commentary:**
The diagnosis of tuberculosis can be difficult, especially in pediatrics where culture material is often unobtainable and, if obtained, is often not positive because of the paucibacillary nature of disease in children. The majority of current diagnostic tests are sputum-based, which is also a problem for young children with pulmonary TB who do not usually produce sputum, even with induction. Additionally immune-based diagnostics targeting host antibody production or T cell responses may have limitations in immunocompromised patients, such as very young children or HIV-infected children, who are known to be at greater risk for the development of TB disease. Therefore, new diagnostics based upon BSMs secreted by *M. tuberculosis* are particularly attractive since they can enter body compartments outside of the lung, such as blood or urine, and do not rely upon the host immune function to detect. Additionally BSMs could potentially also be utilized to monitor response to anti-TB therapy.

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**From the ACIP Meeting of October, 2015 & February, 2016**

The slide sets and minutes of the October 21, 2015 meeting and slide sets from the February 24, 2016 meeting are available to view. The next ACIP meeting is scheduled for June 22-23, 2016.

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**Welcome to our New SOID Members**

If you know of others who might be interested in joining the Academy and the Section please have them call 1-800-433-9016 ext 5885 or go to www.aap.org. The “Become A Member” link will take them to an application. Current Academy members may join the Section here (member ID and login required). You may also call AAP Customer Services at: 866-843-2271.
Policy Highlights from the Committee on Infectious Diseases (COID)

AAP statements under development
1. Vaccine Exemptions
2. Updated Meningococcal Vaccine Recommendations
3. Infection Prevention and Control in Pediatric Ambulatory Setting
4. Countering Vaccine Hesitancy
5. Adolescent Immunizations
6. Prevention and Treatment of Congenital Toxoplasmosis
7. Infection Control in Organized Sports
8. Biologic Response Modifiers
9. Antimicrobial Stewardship in Pediatrics

Statements in Revision
1. Chemical-Biological Terrorism and Its Impact on Children
2. The Use of Systemic and Topical Fluoroquinolones in Children

The following AAP clinical practice guidelines are in the process of development:
1. Fever in Infants Under 3 Months of Age

Guidelines in Progress with External Organizations
1. HICPAC is working on a guideline for prevention of infections among patients in neonatal intensive care units (NICU)
2. Kawasaki Disease and Endocarditis with Committee on Cardiovascular Disease in the Young (AHA)
3. Diagnosis and Management of Bone and Joint Infections (IDSA/PIDS)
4. Clinical Guidelines for Diagnosis and Antiviral Management of Seasonal and Pandemic Influenza in Adults and Children (IDSA)
5. Infectious Diseases Society of America (IDSA), the American Academy of Neurology Institute (AANI) and the American College of Rheumatology (ACR) clinical practice guideline on Lyme Disease
6. Subcommittee on Babesiosis
7. Clinical Practice Guidelines Practice Guidelines for Outpatient Parenteral Antimicrobial Therapy (IDSA)
What is the common thread among these four diverse presentations?

1. A 2-year-old with otalgia and fever.
2. A 6-year-old with worsening symptoms 10 days into an upper respiratory tract infection (URI).
3. A 5-month-old with bronchiolitis.
4. A 4-year-old hospitalized with an asthma exacerbation.

Answer: They all have human rhinovirus (HRV) and maybe something else too.

HRV is a frequent cause of common colds, but is it an important respiratory virus? HRVs are among the top three viruses detected in children with respiratory illnesses and also among the top 3 detected coincidentally in children with no or minimal symptoms. So if HRV is detected as frequently in nonsymptomatic as symptomatic patients, how important can it be?

**HRV’s role in acute otitis media (AOM) and acute bacterial rhinosinusitis (ABRS).** It is not news that HRV is involved in AOM. HRVs can be detected in the nose of up to one-third of AOM episodes. Up to one-fourth of middle ear fluid (MEF) from AOM contain HRV. Many AOM patients with HRV in the nose or MEF also have bacterial pathogens in MEF. So HRV can cause viral AOM all by itself (up to 12%) and also leads to secondary bacterial AOM in other instances.

The importance of HRVs in ABRS was brought back into focus by a recent publication. These investigators wanted to know what proportion of 4 to 7-year-olds, followed for a year, would develop ABRS following URIs, and what proportion of ABRS episodes had detectable respiratory viruses. They found that URIs occurred at a rate of 1.3 episodes/year, but only 8.8% of URIs resulted in ABRS. Using PCR testing, 81% of all URIs had a detectable virus, with HRV being the most common in ABRS cases. So HRV is as big a player in ABRS as AOM.

**A mechanism of HRV causing bacteria superinfections.** HRV’s predisposition to secondary bacterial function appears to be in part due to its ability to break down the respiratory epithelial protective barrier. HRV does this by breaking an essential part of the tight junctions. Tight junctions are essential for the barrier function of the respiratory epithelium. HRV-exposed epithelial cells lose the integrity of the tight junctions and allow easy penetration of bacteria.

**Cold air exposure makes colds more likely.** HRV grows better at 33°C rather than at core body temperature (37°C). This partially explains why your grandmother was likely correct that exposure to cold air increases the chance of a symptomatic URI. Until recently, better growth at 33°C was thought to be a preference of the virus and explained why HRVs cause URIs (temperature in upper tract is closer to 33°C) more than lower respiratory tract infections (LRTI) where the temperature in lungs is usually 37°C. However recent data show that the better growth at 33°C is really due to a host immune factor. It turns out that respiratory epithelial cells (the target of HRV infection) produce a lot more interferon-alpha when exposed to HRV (a protective innate immune response) at 37°C than at 33°C. The extra interferon more effectively blocks intracellular activities that HRV needs for replication. This means that HRVs can attach to respiratory epithelium both in the upper and lower airways, but replicating/growing will be more likely in the upper airway.

**HRV-C differs from HRV A and B.** Among the 3 types, only A and B can be detected by culture (Figure 1 - See page 18) so, prior to molecular testing type C was not known. HRV-B is detected the least often (Figure 2 - See page 18) but also is the type most detected in asymptomatic patients. While HRV is detected year-round with only mild peaks in fall and spring, HRV-C seems more frequent in deep winter and is associated with pneumonia more frequently than types A and B. 

*Continued on Page 18*
B. (Figure 3 - See page 19) All types are associated with asthma, but HRV-C has also been more frequently associated with severe wheezing and asthma admissions.5

Types A and B use the same adhesion molecule, ICA M-1, on human respiratory epithelium as a receptor, or docking point, to initiate infections. HRV-C uses a different adhesion molecule as a receptor, CDHR 3. (Figure 4 - See page 19) What makes this interesting is that HRV-C attaches more readily to the respiratory epithelium of children with a single nucleotide mutation in the CDHR-3 gene. These children also have particularly severe exacerbations of asthma.6 Further, the mutation seems to allow HRV-C infection with exposure to less virus particles.

HRV and pneumonia. HRV-C attaching more readily to respiratory epithelium may also explain reports of pneumonia occurring more often with type C and even with only low HRV-C viral loads. This contrasts with HRV-A, which appear to usually have high viral loads. One could postulate that HRV-A needs more virus particles concurrently in the lower respiratory tract (higher viral load) to overcome the temperature-dependent host defenses (higher interferon production) and thereby to cause LRTI.7 With lower viral inocula, HRV-A would be restricted by the host defenses to the upper airway.

HRV vs. RSV in Bronchiolitis.
While these are intriguing thoughts related to HRV pneumonia, viral load does not appear to differ between HRV types when causing bronchiolitis or even be associated with disease severity. This differs from RSV where high viral load is associated with more severe RSV bronchiolitis.

But wait – there’s more about RSV and HRV bronchiolitis. It seems that bronchiolitis is more likely to relapse when caused by an HRV/RSV coinfection (odds ratio: 1.54; 95% CI 1.03-2.30; P = 0.03) than when caused by either HRV alone or RSV alone.8 Of note, when either HRV or RSV is the sole pathogen, HRV seems to cause bronchiolitis in older children than does RSV.9 The children with HRV alone had a median age of 13 months vs. a median of 5 months for those with RSV alone; and patients with bronchiolitis due HRV alone more often had atopic dermatitis (odds ratio, 16.7; 95% confidence interval, 2.22-100) and blood eosinophilia (odds ratio, 2.22; 95% confidence interval, 1.04-50).

HRV Persistence on fomites. As a practical aspect, the presence of several hundred serotypes within genotypes A, B and C mean that we all will be susceptible to some of the HRV that circulate each year. With no effective antivirals available, prevention is the best strategy. Hand hygiene and cough etiquette are reasonable approaches. Cleaning surfaces is also important because HRV can survive at room temperature on fomites up to 48 hours in low humidity and longer with either high humidity or when in secretions that contain salt or protein.10

Summary: HRVs are increasingly detected due to new diagnostic technology. HRV-A and C are more common than HRV-B, which is less likely to produce symptomatic disease. HRV-C differs fundamentally from HRV-A and appears to
take advantage of a host mutation in the HRV-C receptor in some patients, particularly those with severe asthma. HRV commonly causes not only outpatient URIs but also bronchiolitis, hospitalized pneumonia under five years of age, and asthma exacerbations in those with pre-existing asthma. Sequelae due to HRV are common, both short-term and long-term. Short-term sequelae include bacterial AOM and ABRS. Long-term sequelae include asthma later in life after early-childhood HRV infection. So, HRV is more than just a cause of the common cold. It is an important respiratory virus.

Final caveat– like enterovirus, HRV detection can occur weeks after symptoms of the original HRV infection ceased, so it may be that symptoms that are present at the time of HRV detection may really be due to something else.

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**Figure 3.** Chest X-ray interpretations in HRV type C than HRV type A patients. (4)

**Figure 4.** Human rhinovirus (HRV) attaches to host respiratory epithelial cells by docking its “canyon” to an adhesion molecule receptor. ICAM-1 serves as receptor for HRV-A and B, while CDHR-3 is receptor for HRV-C.
ID Pearls and Other Gems: Human Rhinovirus . . . Continued from Page 19

References:


New MOC Part 4 Activity:
EQIPP Judicious Use of Antibiotics module

This new course will be released in April 2016! You can sign up to receive a notice when this course becomes available if you visit: http://eqipp.aap.org/
Greetings from the Lone Star State! 2015 was an exciting year for our Committee. Our committee membership continues to remain high. With currently 38 members [31 general pediatricians/infectious disease specialists, 4 students, and 3 public health consultants], we represent a wide variety of stakeholders, expertise and priorities. To stay organized, our committee holds in monthly 30 minute phone conferences. Participants include committee members as well as representatives from Texas Pediatric Society (TPS), Department of State Health Services (Texas) and Texas Medicaid.

**Surveillance activities:** The monthly conference phone calls have been especially valuable during the many high-priority local and national infectious disease outbreaks occurring over the past year (Ebola, Disneyland Measles Outbreak, Enterovirus D68). In addition, our respiratory syncytial virus (RSV) regional surveillance data (https://www.dshs.state.tx.us/IDCU/disease/rsv/Data.doc) is reviewed twice monthly, via phone conferences, during our winter season, which is especially important in shaping palivizumab usage policy. In particular, our committee supported a change in the Texas Medicaid's palivizumab administration policy to match AAP recommendations for the 2015-2016 RSV season.

**Human papilloma virus (HPV) vaccine advocacy:** We are particularly excited about efforts by our committee on HPV. In June 2015, TPS assisted the University of Texas MD Anderson Cancer Center to host a ‘Summit on HPV-Related Diseases’ in Houston and conduct an environmental scan on HPV vaccination in pediatric care settings in Texas. Furthermore, our chapter was awarded an AAP Hub and Spoke HPV Quality Improvement Grant. Practices from AAP District VII will collaborate in a four month project to increase HPV vaccine initiation rates. TPS also was awarded an AAP grant supported by Merck. Through this grant, we are sponsoring an upcoming half-day seminar in San Antonio on improving HPV vaccination rates, and will be joining forces with many other statewide professional organizations, academic institutions, and governmental public health agencies for implementing Texas’ HPV vaccine strategic plan to significantly reduce morbidity and mortality from HPV-associated cancer.

**Legislative activities:** The committee was involved in the 2015 Legislative Session in Texas. House Bill 2171 (“Easy Access to Adult Shot Records”), which extends the age an adult can consent to keep their immunization records in our state registry (ImmTrac) from 18 to 26 years was passed (effective 9/1/15) as well as the House Bill 2055 (“Emerging and Neglected Tropical Diseases”) which creates a system to identify the incidence of neglected tropical diseases (NTDs). Cysticercosis, cutaneous leishmaniasis, dengue and Chagas disease are widespread in South Texas and even in Houston (Hotez, P. Ten Global “Hotspots” for the Neglected Tropical Diseases. PLoS Negl Trop Dis 2014 May 29;8(5):e2496). This surveillance system will be a critical tool to monitor and respond to NTDs. Both bills were supported by our committee.

**Future efforts:** Areas of opportunity for our committee include increasing transparency for school campus-specific vaccine exemption rates. Over 40,000 students in Texas opted out of vaccinations using personal belief exemptions (PBEs) in 2014, a trend which has increased 17 fold since PBE were first allowed in our state in 2003. Consequently, our committee is engaging stakeholders on clinics dismissing vaccine refusers. In addition, we are supporting efforts to make our ImmTrac vaccine registry an ‘Opt-Out’ process. Furthermore, we are hoping to build momentum (as done in New Jersey and Connecticut) to mandate influenza vaccine for children age ≤ 5 attending daycare facilities.

We are looking forward to another great year!

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New Policy/Guidelines

Andrea Sperduto, MD FAAP
Cleveland Clinic Foundation

Besides the individual web sites listed below, links to the AAP ID policies, IDSA policies and the CDC ID Recommendations and Reports are all available at the SOID website: http://www2.aap.org/sections/infectdis/policy.cfm

1. AAP
      Lists specific changes but not actual schedule.

2. MMWR
The most up to date information regarding Zika can be obtained as it is updated on the CDC's Zika Webpage and the MMWR Zika Reports.

      i. Modes of transmission under investigation.
      ii. Primary transmission via bite of Aedes species mosquito.
      iii. Transmission from mother with viremia to infant, sexual transmission and lab exposures.
      iv. Theoretical transmission risks are through blood transfusions and organ/tissue transplantation.
      v. There has been no evidence for transmission through breastfeeding, although Zika virus RNA has been found in breast milk.
      vi. Incubation period is under investigation but currently thought to be 3 days to 2 weeks.
      vii. Symptomatic disease is generally mild and is characterized by 2 or more of the following (acute onset fever, rash (pruritic or maculopapular), arthralgias, or nonpurulent conjunctivitis.
      viii. Spectrum of disease in neonates infected in perinatal period is unknown. 2 cases have been reported (1 asymptomatic and other with thrombocytopenia and diffuse rash).
      ix. Available data on mosquito-infected infants and children indicate that most are asymptomatic or have mild disease similar to adults.
      x. Deaths from Zika virus in all ages appear to be rare.
      xi. Guillain-Barré syndrome has been reported following Zika virus infection but currently no causal link.
      xii. Guidelines are included for:
         a. Evaluation and testing of infants with possible congenital Zika virus infection.
         b. Evaluation and management of infants and children aged <18 years with possible acute Zika virus disease.
         c. Breastfeeding for mothers with Zika virus infection is encouraged currently since the benefits outweigh theoretical risks.
         d. Prevention of Zika virus infection through use of insect repellants, long sleeve clothing and screening.

   b. Update: Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure - United States, 2016. MMWR February 12, 2016/65(5);122-127.


   d. Interim Guidelines for Pregnant Women During a Zika Virus Outbreak- United States, 2016. MMWR January 22, 2016/65(2);30-33.

Continued on Page 23
e. Advisory Committee on Immunization Practices Recommended Immunization Schedules for Persons Aged 0 through 18 Years - United States, 2016. MMWR February 5, 2016/65(4);86-87.

The schedule as a pdf can be accessed at: http://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf

f. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 years or older - United States, 2016. MMWR February 5, 2016/65(4);88-90.

g. Update: Shortened Interval for Post vaccination Serologic Testing of Infants Born to Hepatitis B-Infected Mothers. MMWR October 9, 2015/64(39);1118-1120.
i. Shortened to 9-12 months from previous 9-18 months (or 1-2 months after final dose of the vaccine series).

h. Use of Serogroup B Meningococcal Vaccines in Adolescents and Young Adults: Recommendations of the Advisory Committee on Immunization Practices, 2015. MMWR October 23, 2015/64(41);1171-1176.
i. Men B series may be administered to adolescents and young adults aged 16-23 years to provide short-term protection against most strains of serogroup B meningococcal disease.
ii. Category B recommendation (individual clinical decision).

i. Intervals Between PCV13 and PPSV23 Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR September 4,2015/64(34);944-947.

j. Licensure of a Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine and Guidance for Use as a Booster Dose. MMWR September 4, 2015/64(34);948-949.
i. Quadracel (Sanofi Pasteur) was licensed March 24, 2015 for use in children aged 4-6 yrs.

3. IDSA

i. Statement updates 2005 iteration.

i. Updates 2009 guidelines.
ii. Summarizes treatment recommendations for nonneutropenic and neutropenic patients with various clinical diseases and under various circumstances.
iii. Guidelines were reviewed and endorsed by AAP and PIDS.
iv. Detailed descriptions of methods, background and evidence that supports each recommendation can be found on IDSA website: http://www.idsociety.org/Organism/#Fungi

i. Updates info on Bacterial Enteric Infections (salmonella, shigella, campylobacter, E. coli and clostridium difficile).
ii. Risk of bacterial diarrhea varies with CD4 count and is greatest in those with clinical AIDS and/or <200 CD4 cells/mm³.
New Policy/Guidelines  Continued from Page 23

4. HIV Guidelines

Complete guidelines and information can be found at: [http://aidsinfo.nih.gov/guidelines](http://aidsinfo.nih.gov/guidelines) and are updated periodically.

a. Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents.
   i. Updated January 28, 2016.
   ii. Based on two large randomized, controlled trials.
   iii. Antiretroviral therapy (ART) should be initiated for all HIV-infected patients regardless of CD4 count.
   iv. Although the 2 trials did not include adolescent patients, it is recommended that they be started on ART as soon as possible since they should derive benefits as did the adults.

b. Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents.
   i. Updated August-December 2015.
   ii. Included are updates on Syphilis testing and treatment, Candida treatment, CMV retinitis, Toxoplasmosis treatment, HPV screening for women and use of the HPV vaccine, how to manage Chagas treatment failures, HSV suppressive treatment with acyclovir, and when to start ART in patients undergoing Cryptococcosis therapy.

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**ID Sessions at the Pediatric Academic Societies Meeting – Baltimore, Maryland on April 30 – May 3, 2016**

For the descriptions of the ID sessions go to: [http://www.pas-meeting.org/tracks/tracks_ids.asp](http://www.pas-meeting.org/tracks/tracks_ids.asp)

For the complete PAS meeting schedule go to: [https://www.pas-meeting.org/schedule/schedule.asp](https://www.pas-meeting.org/schedule/schedule.asp)

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**SOID Travel Grant Awards**

The Section is pleased to offer NCE travel grants for the 2016 NCE to residents with an interest in infectious diseases or ID fellows in training who are AAP/SOID members. Complete the [application](http://www.pas-meeting.org) and submit it by May 6, 2016 to lrutt@aap.org
THE SECTION ON INFECTIOUS DISEASES

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