Greetings, SOID Members! I hope that everyone had a wonderful summer and have taken time to be outdoors and enjoy the sunshine. It is hard to believe that fall is already here. This is the last letter that I am writing as Chairperson of the SOID. It has been an absolute honor and privilege to serve as Chairperson of this vibrant section and I want to thank all the members for their support and wonderful suggestions for improving the educational programs that we provide. I want to congratulate Dr. Ken Zangwill on being selected as the incoming Chair of the SOID. He will do a great job.

I would also like to welcome Dr. Ingrid Camelo to the SOID Executive Committee as the second Training Fellow Liaison. Dr. Camelo is currently a second year pediatric infectious diseases fellow at Boston University Medical School/Boston Medical Center. Dr. Robert Frenck was elected to a second, three-year term on the Executive Committee and will assume the role of the Education Subcommittee Chair for the section. Dr. Anne Rowley will complete her term as the Planning Group Representative for pediatric infectious diseases at the conclusion of the 2018 National Conference. The SOID Executive Committee very much appreciates Dr. Rowley’s collaboration and support in the development of educational sessions. Congratulations to Dr. Mary Anne Jackson who was appointed to assume the Planning Group Representative position for pediatric infectious diseases going forward.

The SOID Executive Committee is pleased to award the 2018 Award for Lifetime Contribution in Infectious Diseases Education to Dr. James Cherry in recognition of his outstanding commitment to the education of pediatricians on infectious diseases. Dr. Cherry
Chair’s Letter Continued from Page 1

is most deserving of this honor. The 2018-2019 S. Michael Marcy Visiting Professor Program awardee is the University of California San Francisco at Fresno Pediatric Residency Program. The visiting professor who they have selected is Dr. Mary Anne Jackson. Congratulations to the award winners.

In 2018, the SOID will sponsor 18 general infectious diseases-related sessions at the 2018 National Conference in Orlando, Florida. In addition, the SOID will also be co-sponsoring sessions with the Section on Epidemiology, Public Health and the Evidence, the Disaster Preparedness Advisory Council and the Section on Adolescent Medicine. For 2019, 17 general infectious diseases sessions were accepted for the National Conference. The SOID will also be collaborating with the Sections on Allergy and Immunology and the Section on Otolaryngology and Head and Neck Surgery on their programs.

August was national immunization month so hopefully everyone had a chance to review their immunization policies and found innovative ways of reminding their patients and families on the importance of being up to date on their immunizations. This is especially important for the adolescent population as immunization rates for the recommended vaccines have been slow to increase. Given the severity of the 2017-2018 influenza season with 180 pediatric deaths (80% were not vaccinated) and thousands of hospitalizations, the CDC and the AAP are strongly recommending that influenza vaccination be administered as soon as possible once it is available. There are a number of updated recommendations regarding influenza vaccination and I encourage everyone to review the AAP Policy Statement on the “Recommendations for Prevention and Control of Influenza in Children, 2018-2019” in Pediatrics 2018;142(4):e20182367. Even though the influenza vaccine is not perfect, studies have shown that it significantly reduces the risk of severe influenza and deaths and we as pediatricians need to continue to be strong advocates for the use of this and other vaccines and serve as a credible educational resource on vaccines to the community.

I encourage you to spread the word to your colleagues who may have an interest in the SOID and its activities to join the Section. I would also like to encourage all members who are interested in volunteering on the SOID and/or who have suggestions regarding educational topics, website content or the newsletter content to please contact us or complete the 8-question expertise and interest survey.

The SOID very much looks forward to receiving your ideas and suggestions as we go forth and thank you for your continuing interest and membership. Please don’t hesitate to contact Suzanne Kirkwood, the SOID manager and staff liaison at the AAP (SKirkwood@aap.org) to let us know how we can best serve your needs.

Thank you again for all your support. Best wishes for great fall and winter.

With warmest regards,

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

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.
Section on Infectious Diseases Award for Lifetime Contribution In Infectious Diseases Education

The SOID Executive Committee is pleased to award Dr. James Cherry the 2018 Award for Lifetime Contribution in Infectious Diseases Education in recognition of his outstanding commitment to the education of pediatricians regarding infectious diseases. Dr. Cherry is currently a Distinguished Research Professor of Pediatrics at the David Geffen School of Medicine at UCLA and Mattel Children’s Hospital at UCLA, Division of Infectious Diseases.

Following his infectious diseases fellowship training, Dr. Cherry established one of the first formal pediatric infectious diseases fellowship programs in the world in 1963 at the University of Wisconsin. In 1973 Dr. Cherry started the first pediatric infectious diseases training program at UCLA. During his 43 year tenure at UCLA, numerous trainees have gone on to be leaders in pediatric infectious diseases in the United States and in other countries throughout the world.

Throughout his career, Dr. Cherry has received numerous national and international awards including: The John and Mary B. Markle Scholar in Academic Medicine; Distinguished Physician Award of the Pediatric Infectious Diseases Society; The Stanley A. Plotkin Lectureship in Vaccinology of the Pediatric Infectious Diseases Society; and the European Society for Pediatric Infectious Diseases Bill Marshall Award.

Dr. Cherry’s laboratory experience has been instrumental in improving our understanding of virology, mycoplasma, and the serology and molecular microbiology relating to Bordetella species. His main research over the last 50 years has been related to vaccines and vaccine preventable disease (especially measles, rubella, influenza, smallpox and pertussis). Another major interest and passion of Dr. Cherry relates to pertussis epidemiology and pertussis vaccines.

Dr. Cherry has published 302 research papers, 108 editorials and commentaries, and 282 book chapters. He is the senior editor of the Feigin and Cherry’s Textbook of Pediatric Infectious Diseases, now in its 8th edition, which serves as a definitive source of information about common and rare conditions, particularly for its fine detail about the pathophysiology of infectious diseases. In the first 7 editions, Dr. Cherry not only acted as editor but personally contributed about 20 chapters to the book.

In addition to the textbook, for the last 5 decades, Dr. Cherry has been a much sought after national and international speaker who has spoken at countless plenary sessions, invited professorships, and other presentations across the country and around the world on topics as varied as pertussis, influenza, poliomyelitis, immunization against smallpox, and the fetal consequences of Zika virus infection. In recent years, he has continued to advocate both in California and nationally for childhood vaccination, providing an effective voice of clarity about the benefits of immunizations and the dangers posed by pertussis, measles, and other vaccine preventable diseases. Through his participation and contributions to innumerable infectious diseases educational programs, his ground-breaking lab research, his textbook and his efforts to address misconceptions about vaccines, Dr. Cherry has been a pioneer in the field of Infectious Diseases and is most deserving of the SOID 2018 Lifetime Contributions Award in Infectious Diseases Education. Please join us in congratulating Dr. Cherry on his award!

The award presentation for Dr. Cherry will be held at the Meet the Red Book Committee session (session S3021) on Monday, November 5, 2018 at 8:00 a.m. at the AAP National Conference and Exhibition in the Orange County Convention Center in room W303.

From the ACIP Meeting of June, 2018

The slide sets and minutes of the June 20-21, 2018 meeting were not yet available but will be available here. The next ACIP meeting is scheduled for October 24-25, 2018.
Welcome to Our New Training Fellow Liaison

Ingrid Camelo, MD, MPH, FAAP received her medical degree from the military University Nueva Granada in Bogota, Colombia. She completed 2 years of pediatric residency training at Louisiana State University and transferred to University of Vermont after hurricane Katrina. Dr. Camelo is currently a second-year Pediatric Infectious Diseases Fellow at Boston Medical Center in Boston, Massachusetts. She completed a Master of Public Health from University of Vermont and has worked in the past with residents and students during her work as a pediatric attending at University of Vermont spending time both mentoring and teaching. She is especially interested in global health and has worked in Africa in the past conducting research which can be used as a teaching tool and decision aide in resource limited countries for better diagnosing lower respiratory tract diseases.

ID Training Fellows Column:
Adolescent Immunization Platform

Sophie Katz MD, FAAP
SOID Executive Committee Training Fellow Liaison, Vanderbilt University School of Medicine, Nashville, TN

Katherine Richardson MD, FAAP
SOID Education Subcommittee Training Fellow Liaison, Children’s Mercy Hospital in Kansas City, MO

What would you do in these situations? Read the following questions to test your knowledge about adolescent vaccines. Answers/discussion points can be found in the text below.

1. It’s late September and you’re eager to give your first dose of influenza vaccine for the year. When you offer the vaccine, your patient’s mother says “My whole family got the flu shot last year, and we all got the flu. Why should we get it again this year if it doesn’t work?” You respond with:
   a. State that the vaccine significantly reduces the risk of pediatric mortality from influenza illness
   b. Agree with the mother and note that it’s better not to get vaccinated this year
   c. Tell the mother that the flu vaccine usually provides about 15% of protection from influenza illness
   d. Commiserate with the mother, and comment that the National Institute of Allergy and Infectious Diseases (NIAID) currently has no initiatives to encourage development of a universal flu vaccine

2. A 15 year old male presents to your clinic for an acute visit for URI symptoms. You notice he has not had a physical in the last 3 years due to missed appointments and is behind on immunizations. Your thoughts regarding getting him caught up on vaccines include:
   a. Ask him and mother how they feel about getting caught up on vaccines today
   b. Plan to schedule a well-child visit at which to administer catch-up vaccines
   c. State that part of your plan for today’s office visit is to provide catch-up vaccines
   d. State that since he is sick you will not give shots today but will schedule a follow up for him to receive vaccines in 1 week

3. You’re seeing a 12 year old boy for his annual sports physical. The patient’s mother states that she wants “only the shots he needs to attend school” to be provided today. Your response to this is:
   a. Agree with the mother as this is exactly what you were planning on providing as the HPV vaccine is not necessary
   b. PComply with mother, knowing that the patient should start HPV vaccination
   c. State that in addition to the vaccines he needs for school enrollment, the patient should also start HPV series
   d. State that this is fine because her son won’t be sexually active for a couple of years and therefore you can wait before administration of HPV vaccine

Continued on Page 5
4. A mother brings her 11 year old daughter in for a well-child check. The mother and daughter state that they have seen public service announcements about the HPV vaccine, but the patient’s mother is also worried about sexual promiscuity with HPV vaccine. You plan to tell them:

a. If she starts the vaccine series prior to age 15 years, she will only need 2 doses of vaccine as there is better immune response in younger patients
b. The vaccine is safe and effective for males and females and prevents cancer
c. There are no increased rates of sexual promiscuity amongst teens who are vaccinated against HPV versus those who are not
d. All of the above

Background


<table>
<thead>
<tr>
<th>Table 1. Adolescent Vaccine Recommendations, 2018</th>
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<tbody>
<tr>
<td>11-12 years of age</td>
</tr>
<tr>
<td>Meningococcal (MenACWY) – one dose</td>
</tr>
<tr>
<td>Tetanus, diptheria &amp; acellular pertussis (Tdap) – one dose</td>
</tr>
<tr>
<td>Human papillomavirus (HPV) – two doses</td>
</tr>
<tr>
<td>16 years of age</td>
</tr>
<tr>
<td>Meningococcal (MenACWY) – one dose</td>
</tr>
<tr>
<td>Meningococcal B (Men B) – two doses*</td>
</tr>
<tr>
<td>*Based on clinical discretion for otherwise healthy adolescents</td>
</tr>
<tr>
<td>Adolescents of all ages</td>
</tr>
<tr>
<td>Annual influenza vaccination</td>
</tr>
<tr>
<td>Review immunization records, administer catch-up vaccines if needed</td>
</tr>
<tr>
<td>Review medical history, administer additional vaccines as needed based on increased risk due to underlying condition or increased risk of exposure</td>
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</table>

While adolescent immunization coverage has improved in the past decade, opportunities remain to optimize overall immunization rates and series completion in this age group. The National Immunization Survey-Teen (NIS-Teen) is an annual survey that collects data on vaccines received by adolescents aged 13-17 years in the United States (U.S.). Recent NIS-Teen data demonstrate that overall adolescent vaccination coverage continues to improve for coverage with HPV vaccine and MenACWY, and remains high for ≥ 1 dose of Tdap. HPV vaccination initiation has increased an average of 5.1 percent annually since 2013, but substantial gaps remain with regards to HPV vaccination practices. Vaccination coverage with HPV vaccine is approximately 25% lower than coverage with Tdap or MenACWY (Figure 1). Barriers to adolescent immunization include infrequency of healthcare visits, a lack of awareness among parents and adolescents, and missed opportunities for vaccination.
Recommended Vaccines for Adolescents

Meningococcal Vaccines

In infants and children younger than 5 years, approximately two thirds of meningitis cases are caused by serogroup B, whereas serogroups C, Y or W are implicated in approximately two thirds of cases among persons 11 years of age and older. Although the overall incidence of meningococcal disease has been declining in recent years, outbreaks continue to occur. Two polysaccharide-protein conjugate vaccines are currently licensed for use in the U.S.: MenACWY-D (Menactra; Sanofi Pasteur Inc, Swiftwater, PA) and MenACWY-CRM (Menveo; Novartis Vaccines, Cambridge, MA). Both vaccines provide protection against serogroups A, C, W, and Y. An additional MenACWY polysaccharide vaccine (Menomune; Sanofi Pasteur Inc, Swiftwater, Pennsylvania, US) was discontinued in 2017 in the U.S. The AAP and ACIP currently recommend vaccination with a single dose of either MenACWY vaccine at age 11-12 years, with a booster dose at age 16-18 years.

Two meningococcal B vaccines have been licensed in recent years (Bexsero; Novartis Vaccines, Cambridge, MA and Trumenba; Wyeth Pharmaceuticals, a subsidiary of Pfizer, Philadelphia, PA). The AAP and ACIP currently recommend the use of either MenB vaccine for people 10 years and older at increased risk for meningococcal serogroup B disease, such as persons with asplenia, sickle cell disease, persistent complement component deficiency (including eculizumab use), or during a serogroup B meningococcal disease outbreak. Adolescents not at increased risk who desire MenB vaccine may be given the vaccine based on clinical discretion. A recently published article in Pediatrics notes that primary care physicians have significant knowledge gaps about MenB disease and the MenB vaccine, which drives the decision not to discuss the vaccines at routine well child checks. Of note, the two licensed vaccines are NOT interchangeable, and subsequent doses should be continued with the same brand initiated.
Acellular Pertussis Vaccines

Despite high vaccine coverage, there has been a resurgence of pertussis cases in the U.S. The incidence of pertussis peaked in 2012, with approximately 48,277 cases reported across all ages. In 2017, only 15,808 cases were reported across all age groups, with 33% occurring in adolescents aged 11-19 years. Because vaccine immunity wanes after just a few years after vaccine receipt, adolescents are recognized as an important reservoir for pertussis, so the AAP and ACIP recommend immunization with a single dose of Tdap for persons aged 11-18 years. If adolescents present with a wound requiring tetanus vaccination and the patient has not already received Tdap, it can be given at this presentation and count towards vaccine administration if the adolescent is aged 11-18 years. Pregnant adolescents and their partners should also receive Tdap with each pregnancy, between 27 and 36 weeks of gestation.

Influenza Vaccines

A total of 179 influenza-associated laboratory-confirmed influenza-associated pediatric deaths occurred during the 2017-2018 influenza season in the U.S. The CDC conducts annual reviews to determine vaccine effectiveness, and recent studies show that influenza vaccination typically reduces the risk of influenza illness by approximately 50% and significantly reduces risk of pediatric mortality from influenza. In the 2017-2018 season, the influenza vaccine demonstrated an overall 36% vaccine effectiveness, with 42% effectiveness against B strains, 67% against H1N1 and 36% against H3N2.

Annual vaccination against influenza is recommended for all persons age 6 months and older. While the ACIP has approved the use of any licensed, age-appropriate influenza vaccine without preference for any influenza vaccine product, the AAP recommends inactivated influenza vaccine (IIV3/4) as the primary choice for all children because effectiveness of the intranasal live attenuated influenza vaccine (LAIV4) was inferior against A/H1N1 during past seasons and is unknown against A/H1N1 for this upcoming season, though it may be considered in children who would not otherwise receive influenza vaccine. All children with egg allergy of any severity can receive an influenza vaccine without any additional precautions. In February 2018, the National Institute of Allergy and Infectious Diseases (NIAID) announced its Universal Influenza Vaccine Strategic Plan, outlining the institute’s priorities in developing a universal influenza vaccine that provides robust, long-lasting protection against multiple subtypes of flu.

HPV Vaccines

An estimated 31,500 newly diagnosed cancers in men and women are attributable to HPV annually, and approximately 90% of these could be prevented by the nine-valent HPV vaccine (9vHPV). The AAP and ACIP currently recommend routine vaccination for all adolescents at 11-12 years of age, although the series can start as early as 9 years of age. The 9vHPV is the only HPV vaccine currently used in the United States. In addition to HPV types 6, 11, 16, 18 (known to cause 63% of cervical cancer and anogenital warts) contained previously in the HPV4 vaccine, the 9vHPV vaccine includes HPV types 31, 33, 45, 52 and 58, which are known to cause an additional 10% of cervical cancers.

The number of vaccine doses depends on age at vaccination: a 2-dose series is recommended for children age 9-14 years at initiation, while a 3-dose series is recommended for those >15 years of age at initiation. Recommendations for completion of the vaccination series depend on the age of initiation. For example, if the first dose is given at 9-14 years, the individual only needs 1 more dose ≥ 6 months later to complete the series, regardless of when the second dose is given. A series begun with quadrivalent HPV vaccine (4vHPV) can be completed with 9vHPV.

More than 97% of healthy vaccine recipients develop antibodies to HPV vaccine types after vaccination. HPV vaccine works extremely well. Eight years after it was first recommended in the U.S., HPV infections responsible for the majority of HPV cancers and genital warts decreased by 71% in teen girls and 61% in young women. In Australia, among women aged 18-24 years, prevalence of HPV types included in the vaccine decreased from 22.7% in the pre-immunization era (2005-2007) to only 1.5% in 2015. Similarly, prevalence decreased from 11.8% to 1.1% among women aged 25-35. With only a 53.3% 3-dose coverage rate, these substantial decreases in prevalence indicate the presence of strong herd immunity and effectiveness of less than 3 vaccine doses. Studies have not found evidence of waning protection over the past 10 years. HPV vaccines have not been proven to have therapeutic effect on existing HPV infection or disease and do not offer protection against progression of infection to disease from HPV acquired before immunization. Therefore, HPV vaccines are most effective when administered before most people are exposed to HPV through sexual contact.
Optimizing Adolescent Vaccination Rates

There are multiple different strategies that have been implemented to increase vaccine rates amongst adolescents. These different approaches target the provider, the patient, and/or increasing access to vaccination. One important way that vaccine rates can increase is through treating every visit as an opportunity to provide catch-up immunizations. Examples of interventions can be seen in Table 2.

### Table 2. Interventions for Optimization of Adolescent Vaccination Rates

<table>
<thead>
<tr>
<th>Provider-level Interventions</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provider Education</td>
<td>Information on vaccine safety data and disease prevalence</td>
</tr>
<tr>
<td>Provider Feedback</td>
<td>Feedback regarding vaccination rates among a provider’s primary patients</td>
</tr>
<tr>
<td>Electronic Reminders</td>
<td>Flags in an electronic health record reminding a provider to offer a specific vaccine during the patient’s visit</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient-level Interventions</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Reminders</td>
<td>Postcards, letters, phone calls or text messages notifying a patient that they are due for immunizations</td>
</tr>
<tr>
<td>Provider-based Education</td>
<td>Patient/provider discussions regarding vaccines in the ambulatory setting</td>
</tr>
<tr>
<td>Community-based Education</td>
<td>Pamphlets, handouts or commercials detailing vaccine importance</td>
</tr>
</tbody>
</table>

Providers who offer and recommend the HPV vaccine as a routine immunization, without drawing special attention to it, are met with less vaccine hesitancy and have better vaccination rates. School based vaccine programs, reduced cost or free vaccines, and incentives for participation in vaccine program based research can all increase access to vaccination, and thereby improve vaccination rates. Targeting adolescent vaccine administration, especially HPV vaccination, in quality improvement projects can also successfully increase vaccination rates in the ambulatory setting.

### Conclusion

This brief article reviews the latest recommendations regarding immunizations for adolescents. While overall adolescent vaccination rates are increasing, opportunities remain to optimize overall immunization rates and series completion. Healthcare providers can greatly improve these rates by reviewing the immunization history at each adolescent healthcare visit, offering appropriate vaccines, and educating adolescents and their parents regarding the importance of vaccination.

### Answer Key:
1: a  2: c  3: c  4: d

### References:

Continued on Page 10


AAP Adolescent Immunizations Policy & Resources

**Policy:**
- 1. AAP Red Book Online
- 2. Recommended Childhood and Adolescent Immunization Schedules: United States, 2018
- 3. The Need to Optimize Adolescent Immunization
- 4. Practical Approaches to Optimize Adolescent Immunization
- 5. Medical vs. Non-Medical Immunization Exemptions for Childcare and School Attendance
- 6. Countering Vaccine Hesitancy

**Professional Resources:**
- 1. AAP Immunizations Website
- 2. HPV Champion Toolkit
- 3. HPV Hub and Spoke Initiative
- 4. Change Template on HPV
- 5. General HPV Resources
- 6. Communicating with Families
- 7. Provider Resources for Vaccine Conversations with Parents
- 8. Vaccine Preventable Diseases and Policy page

**MOC-CME:**
- 1. EQIPP: Immunizations

**Parent Resources:**
- 1. HealthyChildren.org Articles
Add Your Voice to AAP’s #VoteKids Campaign

The national midterm elections will be held on Tuesday, November 6, 2018, when federal, state and local officials across the country will be elected.

The Academy’s Get Out the Vote campaign, #VoteKids, encourages pediatricians and others who care for children to vote with kids in mind this election. The campaign website, aap.org/votekids, includes information on what’s at stake for children, how and where to register to vote and what you can do to speak up for children at the ballot box.

While children can’t vote, pediatricians and others who care for children can. Please consider adding your voice to these efforts!

The State of the States and Childhood Immunizations: A Call for Advocacy—and Perspective

Some alarming trends on state level immunization rates and rates of nonmedical exemptions have recently emerged (see: http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002578 and https://academic.oup.com/ofid/article/5/6/ofy130/5032316). One important takeaway from these findings are that opt-out rates are variable across and within states, that opt-out rates are rising in some states with less vigorous school entry immunization requirement laws, and that better data collection helps us to understand this variability and intervene accordingly.

A lot has been said about the influence of vaccine skeptic organizations and their high-profile individual members. Rising opt-out rates in some states rates certainly suggest that they have an influence on parental behavior and whether or not children are fully immunized according to recommendations. However, their influence on policymaking requires a more nuanced view.

Make no mistake—vigilance is vital. But while it may be concerning to hear these voices echoed in mainstream politics, it is not resulting in substantive policy change at the state level. It’s also important that their influence not be overstated; in fact, no state has enacted legislation substantially weakening state immunization laws since as far back as 2003.

That track record of success is due squarely to the advocacy of AAP chapters and their advocacy partners, and SOID members can greatly assist these efforts in their own states. The AAP has information and resources to help you, and staff to answer your questions (see below for links to help you to connect with your AAP state chapter, advocate for children, and make a difference).

It is also important to remember that vaccine hesitancy is not the only—or even primary—reason that many children forego routine vaccination. According to Committee on State Government Affairs (COSGA) chairperson, Dr. Gary Wheeler, MD, MPS, FAAP, many children who are unvaccinated have barriers to access to care or competing needs. “We need to continue our efforts to increase the number of providers who give vaccines in low access areas as well as increase regulatory processes to incentivize vaccination for schools and pre-K admission”, Dr Wheeler noted.

Positive reforms of state immunization laws in recent years have had a measurable impact on immunization rates and opt-outs, and there is room for further improvement. Data out of California following implementation of its 2015 nonmedical exemption reform legislation shows:

- The rate of children who entered kindergarten in fall 2016 that were fully vaccinated rose to 95.6%, compared to 92.8% the year prior.
- More kindergartners were vaccinated against measles—97.3% of CA children entering kindergarten had 2 doses of measles vaccine, up from 94.5% the year prior. In the fall of 2014 before the measles outbreak, the rate was just 92.6%.

Bills to expand nonmedical exemptions or to create misleading and ill-intended “risk communication” requirements were introduced in 13 states (HI, ID, IN, MI, MO, MS, NH, NY, OK, PA, TN, WA, and WV) in 2018. Not one was enacted, and little to no procedural action was taken on any of these bills.

Continued on Page 12
In contrast, *bills supporting routine childhood immunizations* — by tightening exemption requirements, requiring that the public be informed about individual school opt-out rates, expanding access to immunization registries, or other positive measures — were introduced in at least a dozen states in 2018 (AL, AZ, FL, HI, ID, KS, LA, ME, NJ, NY, OK, and VA). This conforms with the trends in state legislatures over the past several years.

Nevertheless, parents and policymakers continue to be bombarded with anti-vaccine misinformation, though much of it likely originates from outside of your state (see: [https://www.sciencedirect.com/science/article/pii/S0277953617305221?via%3Dihub](https://www.sciencedirect.com/science/article/pii/S0277953617305221?via%3Dihub)). It is critical to help lawmakers in your state understand that these voices are often those of non-constituents, and, in fact, are mostly opposed by the voters that they serve. Recent polling of Texas voters (see [https://www.houstonchronicle.com/news/houston-texas/houston/article/Poll-GOP-voters-favor-child-immunization-laws-13118040.php](https://www.houstonchronicle.com/news/houston-texas/houston/article/Poll-GOP-voters-favor-child-immunization-laws-13118040.php)) demonstrates an overwhelming rejection of these messages. This confirms 2015 Truven/NPR polling data (see: [http://truvenhealth.com/Portals/0/NPR-Truven-Health-Poll/NPRPulseVaccinations_May15.pdf](http://truvenhealth.com/Portals/0/NPR-Truven-Health-Poll/NPRPulseVaccinations_May15.pdf)) finding that over 90% of adults—parents and non-parents alike—agree that children attending public school should be required to receive all recommended vaccinations unless medically contraindicated.

Pediatricians have an essential role to play in this public discussion by lending a calm, yet evidence-based perspective on the safety and efficacy of routine childhood immunizations. You are uniquely qualified to help parents, legislators, and the public at large find reliable information about immunizations from credible sources. Amplifying your own voice through engagement with your AAP chapter is your best way to ensure that you will be heard, and by doing so, children will be better protected from infectious diseases.

**Resources:**

1. AAP Chapters and Districts
2. AAP State Advocacy
3. Immunization Communication Resources:
   - AAP Communicating with Families Web Page
   - CDC Vaccine Conversations with Parents
4. AAP Policy:
   - AAP Red Book Online
   - Medical vs. Non-Medical Immunization Exemptions for Childcare and School Attendance
   - Countering Vaccine Hesitancy

For more information contact Ian Van Dinther, Senior State Government Affairs Analyst at ivandinther@aap.org

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**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 Diseases, Dayton Children's Hospital, Department of Pediatrics, Wright State University Boonshoft School of Medicine, Dayton, OH.

Effective, early treatment of children, especially the very young, who are infected with *Mycobacterium tuberculosis* is critical in preventing the transition from latent tuberculosis (LTBI) to active tuberculous disease. It is imperative to address LTBI given that an
estimated 10% of these infected, untreated individuals will develop active tuberculosis (TB). The current standard 9-month treatment with isoniazid (INH) can be associated with poor adherence rates and potential toxicity. This study compared the safety, side effects, and adherence of 4 months of rifampin (RIF) with 9 months of INH in children with LTBI.

From October 2011 through January 2014, this noninferiority, open-label randomized trial assessed 829 children aged 0 to 17 years of age with LTBI. Patients were enrolled from Australia, Benin, Brazil, Canada, Ghana, Guinea and Indonesia. Children <5 years of age who had a household contact with TB but had negative tuberculin skin test results (<5 mm) could also be enrolled. Individuals in the INH group received a dose of 10-15 mg/kg of body weight once daily for 9 months while those in the RIF group received 10-20 mg/kg of body weight once daily for 4 months. Drugs were administered by the participants or their caretakers. The primary outcome was assessment of serious adverse events resulting in permanent drug discontinuation. Treatment adherence, side-effect profiles, and confirmed active TB were also followed during the 16 months after randomization. Pill counts were performed at all follow-up visits.

All adverse events and active cases of TB were adjudicated by independent panels in a blinded fashion.

The characteristics of the two groups were similar. Of study participants, 128 were <5 years of age and 79 <2 years of age. Complete follow-up was carried out for 98% of the participants. Overall treatment completion was significantly higher among children in the RIF group than among those in the INH group (360/422, 85.3% versus 311/407, 76.4%, respectively). The adjusted difference in completion rates was 13.4 percentage points (95% CI, 7.5 to 19.3). The most common reason for not completing therapy was a decision of children or their parents to terminate the trial drug early. No serious adverse events resulting in permanent drug discontinuation were attributed to either medication. Both regimens had similar low rates of minor symptoms (gastrointestinal symptoms, transient skin reactions, neurologic symptoms, asthenia). No cases of active TB occurred in the RIF group during 562 person-years of follow-up. Two cases of TB were seen in children in the INH group in 542 person-years of follow-up. One of these cases was caused by an INH-resistant organism. Based on the study results, the investigators concluded that 4 months of RIF therapy was safe and had similar rates of efficacy as 9 months of treatment with INH for the prevention of active TB.

Reviewer’s Comments:
Children with LTBI represent a significant challenge towards global TB elimination. These individuals infected with M. tuberculosis are at risk for development of active disease. While there are effective treatments for persons with LTBI, these can be difficult to complete and require resources to sustain the longer duration of therapy. The World Health Organization estimates that only 7% of children in low- and middle-income countries who are <5 years of age with LTBI complete appropriate therapy. The American Academy of Pediatrics’ Red Book notes that there are several treatment regimens available for LTBI, a 4-month course of RIF being one of them. Support for the RIF 4-month treatment regimen, however, has come primarily from reports of use in adults. Of interest, a study published in this same issue of the Journal noted similar results when evaluated in adults with LTBI. Another recently published paper also documented better completion rates with 4-month treatment when used in children. A 4-month course of daily RIF has comparable safety and efficacy as 9 months of INH for the treatment of LTBI in children and further supports the use of this regimen in the pediatric population.

References:


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

Objective: To estimate the prevalence of HSV infections among previously healthy infants ≤ 60 days of age who had cerebrospinal fluid (CSF) bacterial cultures performed in one of 23 participating university-affiliated pediatric emergency departments (EDs) in the US and Canada.
Review of the Recent Infectious Disease Literature.  
Continued from Page 13

**Methodology:** Records of infants ≤ 60 days of age who presented to a participating pediatric ED and underwent CSF evaluation within 24 hours of entering the ED were included. Patient demographics, triage temperature, disposition, length of stay, blood tests, viral culture, HSV typing, polymerase chain reaction (PCR) tests, and antiviral therapy were extracted from the medical record. The primary outcome was the identification of infants with HSV infection defined as viral detection by PCR and/or viral culture from CSF, blood, surface swabs (such as skin, conjunctivae, mouth, or nasopharynx), or other body fluids. HSV disease was classified as skin, eye, mucous membrane (SEM), disseminated, or CNS based on accepted definitions. The frequency of testing and treating was compared across sites.

**Results:** Of 26,533 infants included in the study, 112 (0.42%; 95% CI: 0.35, 0.51%) met criteria for the diagnosis of HSV infection. The distribution of disease classification was relatively equal: SEM – 44, 32 disseminated and 32 CNS. By univariate analysis, HSV-infected infants were significantly younger (median age; 14 days; IQR: 9 -24 days) than uninfected infants (median age: 28 days; IQR: 15 – 41 days). The odds ratio of infection during 0-28 days of life compared to 29-60 days of age was 3.9 (95% CI: 2.4–6.2) and the highest proportion of infections presented during the second week of life.

The median age of infected infants by disease classification was comparable (14-15 days). The rates of positivity for cultures and PCR mirrored disease classification: 100% of SEM infections had culture positivity from SEM, 100% of infants with CNS disease had positive CSF studies and 92% of infants with disseminated disease had positive blood studies; SEM cultures were positive in 63% of infants with CNS disease and 83% of subjects with disseminated disease. Of 97 infected infants with a temperature recorded at triage, 30.9% were febrile (≥ 38oC). Testing and treating empirically varied greatly across sites.

**Conclusions:** The authors conclude that: (1) HSV infection is uncommon among infants ≤ 60 days presenting to the ED and undergoing CSF evaluation, particularly after 1 month of age and (2) the decision to evaluate and treat expectantly is highly variable across pediatric EDs.

**Reviewer’s comments:** This report supports and underscores previous findings from Texas Children’s Hospital\(^1\) that the incidence of HSV infection among infants ≤ 60 days presenting to the ED is between 0.2% and 0.4%. The potentially devastating nature of these infections, particularly if treatment is delayed, creates a dilemma for pediatricians caring for these infants\(^2\). On one hand is the obvious risk to the patient; on the other is the substantial increase in cost incurred by delayed discharge among those patients expectantly treated but without the disease. In the present study, the number needed to treat (NNT) was 237 for all patients included, 152 for infants between 0 and 28 days of age and 583 for infants in the 29-60-day group.

Editorials by Kimberlin\(^3\) and Long\(^4\), published in response to the Texas experience, provide a touchstone for which infants less than or equal to 60 days of age should be evaluated and treated expectantly for possible HSV infection; slight modification is suggested by the present study:

1. Infants 28 days of age or less who present to the emergency room with fever or other signs of suspected sepsis (original recommendation was 21 days)
2. Presence of skin vesicles.
3. New onset of seizures
4. Elevation of hepatic transaminases
5. Presence of symptoms suggestive of sepsis or shock
6. CSF pleocytosis independent of predominate cell type
7. Persistent or recurrent crusting of a scalp electrode site.

A large prospective study of febrile and non-febrile infants ≤ 60 days of age all of whom undergo culture and PCR testing for HSV is required to develop a true predictive rule for these patients.

**References:**

Policy Highlights from the Committee on Infectious Diseases (COID)

AAP statements under development or revision

1. Antimicrobial Stewardship in Pediatrics
2. Chemical-Biological Terrorism and Its Impact on Children
3. Management of Neonates with Suspected or Proven Early-Onset Bacterial Sepsis
4. Tuberculosis Infection in Children: Testing and Treatment
5. Prevention and Management of Perinatal Group B Streptococcal Disease

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

2. HICPAC is working on a guideline for prevention of infections among patients in neonatal intensive care units (NICU)
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
   a. Subcommittee on Babesiosis
6. Clinical Practice Guidelines Practice Guidelines for Outpatient Parenteral Antimicrobial Therapy (IDSA)

Developmental Effects in Children Born to Zika-Infected Mothers: Care, Support, and Services for Children and Families

Authors are Hub Faculty on AAP Project ECHO® Zika:

Steve Caddle, MD, MPH, FAAP, Assistant Professor of Pediatrics at Columbia University Irving Medical Center and Abigail LH Kroening, MD, FAAP, Assistant Professor of Pediatrics at University of Rochester (Rochester, NY).

In 2016, the Brazilian Ministry of Health alerted the international community to the neurodevelopmental effects of congenital Zika virus (ZIKV) after recognizing a surge in cases of congenital microcephaly. The Ministry documented 147 cases of congenital microcephaly in 2014. This number soared to 1950 confirmed cases in 2015, prompting the WHO declaration of ZIKV as a public health emergency. The neurotropic predilection of ZIKV led to a new group of congenitally-infected Children with Special Health Care Needs (CSHCN) that require specialized care and follow-up. Many ZIKV-affected babies are now at key ages for developmental screening, evaluation, and early interventions. Through our work with AAP Project ECHO® Zika, we appreciate the neurodevelopmental complexity of these children and also the resources available to support ZIKV-affected families in the United States (US), US territories (Puerto Rico, American Samoa, US Virgin Islands), and Brazil.

In utero exposure to ZIKV can lead to infants who are asymptomatic, have mild neurodevelopmental abnormalities, or have Congenital Zika Syndrome (CZS). CZS is a constellation of findings including: (1) severe microcephaly with partially collapsed skull, (2) thin cerebral cortices with subcortical calcifications, (3) macular scarring and focal pigmentedary retinal mottling, (4) arthrogryposis (congenital contractures), and (5) marked early hypertonia. Congenital ZIKV infection is also associated with irritability, seizures, dysphagia, optic nerve hypoplasia, hearing loss, and more.

Neurologic injury of this magnitude results in significant developmental delay/disability for infants and children with CZS. Maternal ZIKV infection during the first trimester of pregnancy is associated with the most severe CZS phenotype, although exposure during any trimester incurs risk. Of those infants exposed to ZIKV in utero, nearly half have neurologic/developmental abnormalities identified within the first year of life.
Developmental Effects in Children Born to Zika-Infected Mothers: Care, ... Continued from Page 15

In 2017, the Centers for Disease Control and Prevention (CDC) (in collaboration with the Brazilian Ministry of Health) published results from its ZODIAC (Zika Outcomes and Development in Infants and Children) investigation. The ZODIAC study provided a comprehensive report on 19 children (ages 19-24 months) born during the 2015-2016 Zika outbreak with microcephaly and laboratory evidence of in utero ZIKV infection. Results were striking. Of these 19 toddlers: 15 had severe motor delays (unable to sit independently); 13 and 11 had some degree of hearing and vision loss, respectively; 11 had seizures; 10 had sleep and 9 had feeding difficulties; 8 had been hospitalized at least once since birth (primarily respiratory infections); and 14 of 19 had at least 3 of these findings.4

Cognitive Development. The degree of microcephaly in many of children with in utero ZIKV exposure is severe (e.g., head circumference 3+ standard deviations below the mean). This contributes to significant cognitive delays and a high risk for intellectual disability (greater than 50%) as these children age.5

Motor Development. Motor development is affected by microcephaly and baseline neurologic injury, and complicated if a child also presents with hyper/hypotonia, congenital contractures, or extrapyramidal symptoms. Most infants with CZS have severe motor deficits.

Language Development. Communication is adversely affected by in utero ZIKV infection. The greater the microcephaly/cognitive delay, the greater the language delay. Language development may also be influenced by hearing loss, and oral-motor dysfunction makes speech more difficult.

Social-Emotional and Behavioral Development. Current data suggest that children with CZS show preference for caregivers and some basic social interest, such as through smile.3 Social-emotional delays become more apparent after 4-6 months. Social-emotional development is adversely influenced by increased risk of neuro-irritability, sensory (vision/hearing) losses, and sleep dysregulation.

Overall Development and Function. Children with severe CZS present with significant global developmental delays. Current data suggest that at 12 months chronologic age, most infants with CZS are functioning at 2-3 months developmental age.6 Many with CZS will require life-long care, with limited independence for basic activities of daily living.

In February 2017, the AAP – in partnership with the US Health Services and Resources Administration’s (HRSA) Maternal and Child Health Bureau (MCHB) – launched a national and international-focused collaborative to support health care providers for children affected by the ZIKV epidemic. This collaborative, known as Project ECHO® Zika, offers participants interprofessional telementoring and multi-directional information exchange using the ECHO (Extension for Community Healthcare Outcomes) Model™, which includes structured case-based learning, brief didactics, and discussion.7

Project ECHO® Zika includes participants from several parts of the US, its territories, Brazil, Mexico, Honduras, and Ecuador. To date, clinicians have presented cases on 36 children (0-29 months) with risk or confirmed in utero ZIKV exposure.8 Developmental findings in these children are consistent with previous reports—many have severe microcephaly, structural abnormalities on brain imaging, and seizure disorders. The majority also have ophthalmologic abnormalities, significant feeding difficulties, and irritability. A few have hearing loss. While most children in the Project ECHO® cohort demonstrate social smiles and some visual attention, all demonstrate significant global developmental delays. In our cohort, all children 12+ months chronologic age have developmental ages of less than 6 months.

We still have a limited understanding of how ZIKV affects the developing brain. Some children with in utero ZIKV exposure may not have any discernible effects from this exposure. Other children with in utero ZIKV exposure will have sequelae, but at birth the clinical manifestations of such exposure may range from asymptomatic to severely symptomatic. Researchers describe postnatal ZIKV replication in infant brains, and deceleration of head growth/acquired microcephaly has been documented in some exposed infants.9 It is still unclear why some children with in utero ZIKV exposure will remain asymptomatic, some may later develop microcephaly and other abnormalities, and others will be significantly affected from birth. Researchers are actively investigating maternal and infant risk factors that may explain these differences.10 However, all in utero exposed infants need close medical, developmental, and behavioral monitoring as they age.

Postnatal ZIKV transmission can also occur in infants and children, mainly through mosquito bites, resulting in asymptomatic or mild... Continued on Page 17
Vigilant standardized developmental screening is crucial for all congenital ZIKV-affected infants and children. The AAP currently recommends screening using tools such as the Ages and Stages Questionnaire (ASQ) or the Parents’ Evaluation of Developmental Status (PEDS) at 9, 18, and 24 or 30 month Well Child visits, and ANY time developmental concerns arise.11 For children with severe CZS, delays are obvious and standardized screening highlights relative strengths. For asymptomatic children or children with less severe phenotypes, routine screening is important to disclose areas of need and prompt more in-depth developmental assessment. Asymptomatic or mildly symptomatic children should be screened until school-age and closely monitored thereafter for learning difficulties and behavioral sequelae. In exposed, yet seemingly unaffected children, long term monitoring through adolescence has been advocated to assess for higher-order neurocognitive deficits, such as with executive functioning skills.12 Our colleagues in Brazil, Puerto Rico, and the US Virgin Islands (USVI) routinely use standardized developmental screening to assess infants and toddlers with in utero ZIKV exposure, promptly referring to local resources as indicated.

In the US and its territories, Zika remains a notifiable condition, and the CDC provides guidance to health care providers in collaboration with state, local, tribal and territorial departments of health (DOH). The CDC provides a searchable network of health professionals who care for patients affected by Zika, through Zika Care Connect, as well as Roadmaps to guide parents in monitoring symptomatic or asymptomatic children.13,14

In Puerto Rico, Zika-exposed newborns are enrolled in the DOH’s CSHCN Program. Environmental health programs also provide support services. Apoyo a Padres de Ninos con Impedimentos (APNI or “Support for Parents of Children with Disabilities”) is a Puerto Rico-based non-profit that represents Family Voices and has created a Zika project to empower families of children with or at risk for ZIKV infection.15

In the USVI, approximately 290 infants have been born to Zika-infected mothers15. The AAP-supported Zika Health Brigade was established this year – a partnership between CDC, HRSA, AAP, and the USVI DOH – to offer technical assistance, education, and support to clinicians in the USVI of St. Thomas and St. Croix who care for children with CZS.15 Shana Godfred-Cato, DO, FAAP, describes her experiences in an AAP Voices blog. The islands share one audiologist; a child neurologist and a developmental pediatrician travel to the islands a few times annually for consultations. The USVI Infant and Toddler Program provides territory-wide Early Intervention (EI) developmental services for children 0-3 years. In American Samoa, the DOH provides EI services.

In all US territories, seasonal storms and hurricanes challenge Zika-related support programs. Damaged infrastructure from hurricanes Irma and Maria have fractured communication, prevention efforts, and care delivery.

In Brazil, the Ministry of Health recommends referral to early stimulation programs through the public health system for children from 0-3 years old with CZS.16 Heavily affected cities have established centers with specialized care for children with microcephaly. Several non-governmental organizations assist families in providing CZS evaluations and rehabilitation. Groups such as União de Mães de Anjos (“Union of Mothers of Angels”) provide community-based and social media support for mothers of children born with microcephaly.6

Within the framework of an interdisciplinary team, a family-centered medical home is integral to caring for children with congenital ZIKV exposure. These CSHCN require acute and long-term support that is consistent with the MCHB’s Comprehensive Systems Approach.17

To summarize:

- Some children with in utero ZIKV exposure may not have any effects from this exposure.
- Other children with in utero ZIKV exposure will have neurodevelopmental sequelae that may range from clinically asymptomatic (initially) to severely symptomatic.
- All children with in utero ZIKV exposure require systematic follow-up through school age and adolescence.

Continued on Page 18
As we continue to learn about the range of developmental effects over time, families will benefit from attentive primary care and coordination with specialists, developmental services, and support organizations such as Family Voices and Family-to-Family Health Information Centers. The CDC released new information in August 2018. Additional psychosocial resources are available through CDC and AAP Web sites.18,19

AAP Resources:
• AAP Policy – 2018 Red Book Zika Chapter
• Key Information for Pediatricians
• Resources for Pediatricians
• Psychosocial Support Videos

References:
8. Limjuco S. Dataset from AAP Project ECHO® Zika Case Presentations through June 2018. AAP; 2018.
The utility of serology in diagnosing the cause of three weeks of cough in a teen

Christopher J. Harrison, MD, FAAP, FPIDS, Professor of Pediatrics at the Children's Mercy Hospital and UMKC, Kansas City, MO. Dr. Harrison will be happy to receive contributions from you and, if published, will be duly cited. Please send them to charrison@cmh.edu.

A fully immunized 14-year old male (last pertussis containing vaccine at age 11 years) presents after 17 days of cough. The nearly constant fever up to 38.9°C in the first three days was intermittent up to a week into symptoms. No whoop or post-tussive vomiting were noted, but paroxysm-like episodes occur several times daily often at night. His examination is normal except for a slightly prolonged expiratory phase. His CBC and CRP are unremarkable. Current chest radiograph is normal except for mild peribronchial thickening.

While the differential includes adenovirus, parainfluenza viruses, and Chlamydia pneumonia, Mycoplasma pneumoniae (Mpn) and pertussis are your highest concerns. What is the best approach at this time – culture, serology or PCR or some combination of all? It is important to remember that both of these diagnoses, in the acute setting, have to be made clinically, without laboratory support. The strengths and weaknesses of definitive lab testing follows.

**Mycoplasma pneumoniae**

Mpn testing should only be performed with Mpn compatible presentations (age > 3 years, some wheezing (in a child without asthma), fever longer than 3 days, and cough persisting > 2 weeks) and where results will change the management. Decisions on choice of testing method depends on the duration of illness at presentation.

Mpn culture is not useful here and few if any laboratories do this as a routine test. It is cumbersome, time consuming (up to 3 weeks incubation) and lacks sensitivity at 3 weeks into symptoms. Currently, PCR plus single-sample serological tests are considered reasonable to attempt to diagnose Mpn in symptomatic children by both the US and UK pneumonia Guidelines. But timing of testing in relation to illness onset can increase or decrease the value of either or both test methods.

While PCR (including multiplex assays) is very sensitive early in disease, sensitivity drops dramatically after 3 weeks of illness, leading to false negatives. In one study, only 21% of true cases were PCR-positive. Further, while PCR is becoming a standard for respiratory pathogen detection in some areas, positive mycoplasma PCR results have been noted in asymptomatic children, producing up to 20% false positives.

Mpn serological diagnosis is also problematic. While the diagnostic gold standard for Mpn is serology (fourfold antibody rise in paired sera >three weeks apart), paired sera are not useful for individual acute diagnostic/treatment decisions, being most useful in epidemiological studies for “after-the-fact diagnoses”.

Also, there is no consensus on what constitutes a single-sample confirmatory titer for IgM or IgG partly due to varied results from differing kits and techniques (CFT and ELISA most often). Some results are reported as titers (e.g. 1:4 or 1:64) and some as absorbance units or international units. So, studies with one methodology translate with difficulty to other studies or one’s local methodology.

Low specificity of single-sample testing contributes to the lack of consensus. Initially “positive” Mpn IgM results persist for months, and IgG is detectable for years, leading to false positive results. IgM assay also detect cross reactive antibody to other respiratory pathogens, e.g. Chlamydia pneumoniae, Coxiella burnetti, and other mycoplasma species. The result is that among 3-month to16-year olds, anti-Mpn IgM and IgG antibodies were detected nearly as frequently in asymptomatic children as those with respiratory symptoms. The overall specificity of Mpn IgM in single-sample testing has been 30-45% reducing its utility.

Low sensitivity of Mpn serology also has been noted in the first weeks of infection (IgM in the first week and IgG in the first 2 weeks). By the third week, IgM is most often present and IgG can also be seen in about half by the third week. Even in the fourth week, 20-40% of Mpn infected children will still be IgG negative. So, serology is neither sensitive nor specific without paired sera assays. Nevertheless, commercial and local laboratories often have criteria for what “likely” indicates recent Mpn infection. But this is a case of caveat emptor.
Alternatively, PCR could be useful in the first three weeks of illness. For example, even if serologically “positive” in the first 3 weeks, the patient is not as likely Mpn-infected if the PCR is negative. In contrast, PCR “positive” patients that are seronegative in the first three weeks are likely acutely infected. In another scenario, a positive PCR plus positive serology increases the likelihood of Mpn as the culprit.

It therefore makes sense that both US and UK pneumonia guidelines suggest a combination test approach to Mpn, if results will change management. But remember, only a minority of true cases confirmed by paired testing with 4-fold antibody rise are positive for both PCR and serologically at the time of single sample obtained acutely.\(^6,7\) Therefore, if the index of suspicion is high coupled with an Mpn compatible presentation, it is cheaper to make a presumptive Mpn diagnosis clinically without laboratory testing. Whether empiric antibiotics are useful in this scenario is a whole other discussion.

**Pertussis**

Pertussis serology is even more complicated given the broad spectrum of disease (asymptomatic to lethal) and the background of universal pertussis immunization. The pertussis serology components (pertussis toxin (PT), filamentous hemagglutinin (FHA)) are also in current acellular vaccines that are particularly great at inducing anti-PT IgG for years, despite not being fully protective after 3-5 years. It is reasonable then to worry about false positive serology results; detection of antibody may represent vaccination, recovery from an old pertussis infection, or, of course, acute infection.

When should testing occur? Only patients with known pertussis exposure or with pertussis compatible presentations (by CDC definition, this includes cough >2 weeks plus whoops, paroxysms, or post-tussive vomiting) should be tested. Because PCR is generally at least twice as expensive as serology, it would be nice to be able to use serology for individual patients.\(^11\)

So how to manage a teen 3 weeks into symptoms, possibly due to pertussis? Clinically it can be sound to treat for pertussis based solely on the clinical presentation. But there are public health ramifications to this diagnosis, so do we also just treat all his contacts? We prefer to interrupt potential outbreaks before they begin, so someone would need to survey his contacts/family. Reporting this “probable” case to the Health Department will likely take primary care providers out of the line of fire for decisions on further testing and case finding. But confirmation would be best, and what should the patient and family expect?

“Probable” pertussis can be confirmed by culture or PCR if early in the course (Figure 1). Culture is time consuming at 7-21 days for results and not as sensitive as PCR. But note that CDC still considers culture the gold standard.\(^12\)

There are numerous stand-alone or multiplex FDA-approved pertussis PCR assays, but the most specific assays detect more than one gene, with each gene having only one copy per organism. Previous PCRs targeted a gene with multiple copies per organism and produced too many false positive results.\(^13\) Pertussis PCR’s main weakness is that negative results occur frequently >3 weeks into disease. So, in this teen is serology needed?

Currently, no pertussis serology assays are FDA-approved, yet many ELISAs and multiplex assays using purified non-detoxified PT as an antigen seem reliable (CFT or fluorescent-based assays are not reliable). Paired acute/convalescent serology would confirm infection only after another 3-4 weeks. So, single-sample “acute” testing could be used late in the third week of symptoms (likely 4th week of infection) when sensitivity of both culture and PCR are declining. When the CDC performs its own single-sample serology, samples 2 to 8 weeks into symptoms are preferred, but may be informative out to 12 weeks.

**Figure 1. Relative utility of single sample diagnostic methodologies for confirming pertussis infection.**

Continued from Page 19

Continued on Page 21
Factors confounding interpretation of single sample pertussis serology include nonspecificity of non-Pt antibodies and recent immunization. For example, elevated FHA results may simply be cross-reactive antibodies to non-pertussis Bordetella species, Mpn, C. pneumoniae, or even non-typable Haemophilus influenza. So anti-PT antibodies are better when available.

Yet, antibodies to PT are highest in the first year after immunization and persist for decades, so single sample serology within one year of pertussis vaccine is often impossible to interpret. Commercial laboratories often give guidance e.g. “results indicating levels >95th percentile from their population of adult blood donors” (above the reference range) “are highly suggestive of recent infection or vaccination”. It is unclear how recent the infection needs to be to elevate PT antibody levels in such assays and at times whether locally validated ranges in adults translate well to children.

Given high rates of detection of anti-PT in teens, what would constitute a “positive” result in the teen in question? His last pertussis vaccine was three years prior, so single sample testing appears potentially useful. But what threshold value would indicate that his current illness is most likely pertussis? In Europe, the EU Pertstrain group guideline suggests 50-125 IU/mL titers as indicative of current/recent pertussis infection. However, recent Dutch data show that teens often maintain titers >50 IU/mL for over 3 years post infection and several US studies suggest a higher threshold, ranging from the 2018-21 Red Book’s 100 IU/mL to one study in Massachusetts using 200 IU/mL. Recent Japanese data indicate that almost half of teens have ELISA titers >50 IU/mL while <10% have results >100 IU/mL.

Decision: Almost 4 weeks into symptoms, PCR for either Mpn or pertussis is low yield and expensive. Single sample Mpn serology will likely not be helpful. Single sample pertussis serology may provide actionable data, but turnaround time is up to 5 days, while PCR results return in <24hrs. Given the public health concerns regarding pertussis, it seems reasonable to obtain pertussis PCR. If positive, the diagnosis is confirmed. If negative, pertussis serology should be the next step. Whether to start pertussis treatment at the first visit is a judgment call, but that would be my approach although the benefit to the PCR-negative patient may be minimal.

**Bottom line:** Consider both PCR and single sample serology for pertussis along with pertussis antibiotic treatment. The treatment is empiric if PCR is negative awaiting single sample serology results. If both PCR and single sample serology are negative, then convalescent pertussis serology could still possibly confirm the diagnosis.

**References:**


*Continued on Page 22*


9. Loen and Ieven 2016


11. Pertussis Diagnosis. [https://www.cdc.gov/vaccines/pubs/pinkbook/pert.html#diagnosis](https://www.cdc.gov/vaccines/pubs/pinkbook/pert.html#diagnosis)


ID Sessions at The AAP’s National Conference and Exhibition (NCE) November 2-6, 2018 – Orlando, Florida

The descriptions of the ID sessions sponsored by the SOID are on the Section can be accessed here and the complete conference program can be accessed on the NCE website.

H3076- Section on Infectious Diseases Program

Date: 11/5/2018
Start/End Time: 2:00 PM-4:00 PM
Hours of CME: 1.5

Description: Improving Pediatric Office Preparedness and Addressing Children’s Needs in Infectious Disease Outbreaks and Disasters

Infectious disease outbreaks pose many challenges to pediatric practices. Such outbreaks may be predictable (i.e., seasonal influenza) or sudden and unexpected due to un- or under-immunized children exposed to vaccine preventable diseases or to emerging infections. In such situations, information overload is common and the immediate changes required in the healthcare delivery system can be challenging for doctors and patients. In a round table, interactive format and using real examples from recent outbreaks, this session will offer insight on lessons learned and highlight steps that pediatricians can take to better prepare their practice setting for these events.

Agenda

2:00 PM  Introduction
Moderator: Ken Zangwill, MD, FAAP

2:10 PM  Round Table Topics
1. Practical Infection Prevention and Control Measures
   Craig Shapiro, MD, FAAP
2. The Pediatrician’s Role in Surveillance and Disease Reporting
   Georgina Peacock, MD, MPH, FAAP
3. Effective Communication Strategies with Patients and Families in an Outbreak
   Scott Needle, MD, FAAP; Margaret Fisher, MD, FAAP
4. Vaccine Storage and Access Issues
   Graham Barden, MD, FAAP
5. Helping Families Cope in an Infectious Outbreak Situation
   David Schonfeld, MD, FAAP

3:50 PM  Summary and Wrap-up
Ken Zangwill, MD, FAAP

4:00 PM  Adjourn
New Policy/Guidelines
Andrea Sperduto, MD FAAP
Cleveland Clinic Foundation

I. AAP


Highlights of these updated recommendations include:

- AAP recommends inactivated influenza vaccine (trivalent IIV3 or quadrivalent IIV4) as the primary choice for children. This recommendation was made because quadrivalent live attenuated influenza vaccine (LAIV4) showed inferior effectiveness during previous influenza seasons, and its effectiveness against A/H1N1 is unknown.
- LAIV4 may be used for children who would not otherwise receive an influenza vaccine, if the child is at least 2 years old and healthy with no underlying chronic medical conditions.
- All 2018-19 seasonal influenza vaccines contain a similar influenza A (H1N1) vaccine strain compared with the one that included in the 2017-18 seasonal vaccines. The influenza A (H3N2) and influenza B (Victoria lineage) differ in these vaccines from last year. The quadrivalent vaccines contain the same influenza B (Yamagata lineage) included in last year’s vaccine.
- Children should receive the influenza vaccine as soon as possible after it is available in their community, preferably by the end of October.
- All children with egg allergy of any severity can receive influenza vaccine without any additional precautions beyond those recommended for any vaccine. Egg allergy is not a contraindication for influenza vaccination, nor does it require special consideration.
- Pregnant women may receive IIV at any time during pregnancy, and infants of vaccinated mothers receive protection against influenza and its complications.
- Antiviral medications are important in the treatment and control of influenza, but are not a substitute for influenza vaccination.

This policy statement expands the recommendations in the Influenza chapter in the current edition of *Red Book* (p 476–490).

Also refer to the updated Vaccine Status Table and Influenza Resource pages on Red Book Online.

See related AAP News articles here and below:

- AAP policy emphasizes importance of vaccination after high-severity flu season
- AAP Issues Flu Vaccine Recommendations for 2018-2019

II. MMWR


1. On February 21, 2018 ACIP recommended Heplisav-B (HepB-CpG), a yeast-derived vaccine prepared with a novel adjuvant, administered as a 2-dose series (0, 1 month) for use in persons aged ≥18 years.
2. Seroprotective antibody to hepatitis B surface antigen (anti-HBs) levels were achieved in 90.0%–100.0% of subjects receiving HepB-CpG (Dynavax Technologies Corporation), compared with 70.5%–90.2% of subjects receiving Engerix-B (GlaxoSmithKline Biologicals).
4. HepB-CpG is the 5th inactivated Hep B vaccine currently recommended in the US.
5. Data are limited on interchangeability of this vaccine with other Hep B vaccines.
6. Safety profile is similar thus far to Engerix-B.
7. No data yet available on use in pregnant women.

Continued on Page 25

1. This is a comprehensive report that compiles and summarizes all previously recommendations for the ACIP on prevention and control of pertussis, tetanus and diphtheria in the US.
2. Rationales and background information for the recommendations are explained.
3. Infants and young children should receive 5-dose series of DTaP and one adolescent booster dose of Tdap.
4. Adults who have never received Tdap should receive 1 dose.
5. Women should receive a dose of Tdap during each pregnancy, which should be administered from 27-36 weeks gestation.
6. After receipt of Tdap, adolescents and adults are to receive a booster Td vaccine every 10 years.

D. Update: ACIP Recommendations for the Use of Quadrivalent Live Attenuated Influenza Vaccine (LAIV4) - United States, 2018-19 Influenza Season. MMWR June 8, 2018;67(22)643-645.

1. ACIP recommends that LAIV4 be an option for influenza vaccination of persons for whom it is appropriate for the 2018-19 season.
2. Overview of information discussed that lead to this recommendation is presented.
3. Prior season LAIV4 vaccine had low to no significant effectiveness against Influenza A(H1N1) pdm09-like viruses but was generally effective against influenza B viruses and influenza A(H3N2).
4. The “new” LAIV4 induced higher antibody responses than its predecessor in data from manufacturer.
5. No published effectiveness estimates for this “new” formulation of vaccine against influenza A(H1N1) pdm09 viruses are yet available.
6. Providers should be aware that the effectiveness of the updated or “new” LAIV4 containing A/Slovenia/2903/2015 against currently circulating influenza A(H1N1) pdm09-like viruses is not yet known.

III. IDSA


1. This report updates the 2010 clinical practice guidelines.
2. Recommendations for pediatrics are included, specifically diagnosis and treatment options differ from adults.
   a. Neonates and infants (<12 mos of age) have a high prevalence of asymptomatic carriage of toxigenic C. difficile. Therefore, testing is not recommended.
   b. Children 1-2 yrs of age with diarrhea should only be testing for C. difficile if other infectious and non-infectious causes are excluded.
   c. In children >2 yrs of age, test only those with prolonged or worsening diarrhea and risk factors (eg. underlying inflammatory bowel disease, immunocompromising conditions) or relevant exposures (eg. contact with healthcare system or recent antibiotics).
3. There are insufficient data to recommend screening for asymptomatic carriage and placing asymptomatic carriers on contact precautions.
4. Treatment in children found on Table 2 of guidelines with non-severe initial episode is choice of metronidazole or vancomycin. For severe initial episode or second episode, use of vancomycin is recommended.


1. Included are approaches in patients with different forms of disease (eg. viable parenchymal, single enhancing lesions, calcified lesions, ventricular lesions and subarachnoid.).
2. Children should be managed the same as adults with the same form of disease since there is no evidence to support otherwise.

Continued on Page 26
However, medication dosages should be weight based.

   1. Document developed by experts in lab and adult and pediatric clinical medicine.
   2. Presented in a system-based approach rather than specimen-based, and presented into etiologic agent groups.
   3. Each section contains key points and detailed tables that list suspected agents, the most reliable tests to order, samples and volumes to collect, and if specialized labs are necessary.
   4. Pediatric needs of specimen management are emphasized.

IV. HIV Guidelines
Completed guidelines and information can be found at: http://aidsinfo.nih.gov/guidelines and are updated periodically. Some of the highlights are listed below.
A. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection.
   2. The panel now recommends that all antiretroviral-naive children receive ART, regardless of symptoms or CD4 count.
   3. Updated antiretroviral regimens for initial therapy are made.
   4. Updated regimens that should never be used as part of an ARV regimen (eg. didanosine or stavudine) in an antiretroviral-naive child due to toxicities and safer agents available.
   5. Pediatric drug information Appendix A updated.
B. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV.
   2. Integrase strand transfer inhibitor (INSTI)-based regimens are recommended as initial therapy for most people with HIV.
   3. Monotherapy with any antiretroviral (ARV) drug should not be used due to increased risk of virologic failure and drug resistance.
   4. Links to potential investigational agents for patients with insufficient treatment options due to virologic failure has been added.
   5. Several newer studies now show that those with sustained viral suppression on 3-drugs with no drug resistance may be maintained on 2-drug regimens.
   6. Additional updates on Hep B/HIV coinfection and Hep C/HIV coinfection.
C. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents.
   2. Updated recommendations on HPV and HH-8.
D. Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States.
   2. While the panel does not recommend breastfeeding for women with HIV, a section was added to provide tools to help providers counsel women with HIV on the potential risks associated with breastfeeding.
      a. Women should be counseled on the potential risk of neural tube defects when DTG is taken near the time of conception (6 weeks from last menstrual period).
      b. Table 1 gives more detail recommendations.
      c. Full text guidelines should be reviewed by providers of women regarding this.
SOID Travel Grant Awards

One of the roles of the SOID is to promote the education of those physicians interested in infectious diseases. We are pleased to be able to offer travel grants to AAP members who are residents with an interest in infectious diseases and ID fellows in training. In years when the PREP ID course is held, these travel grants are offered to PID fellows-in training who are AAP/SOID members and will be taking the certifying boards in that year. The following recipients were selected by lottery and received $1,000 to defer travel expenses related to attendance at the 2017 PREP ID course held in Dallas, Texas this past July.

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<tr>
<th>Satja Issaranggoon Na Ayuthaya, MD</th>
<th>Hayley Wilcox, DO</th>
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