Greetings, SOID Members! Hope everyone has been enjoying the relatively mild winter that we are having and have taken time to be outdoors and enjoy the sunshine, even though the Groundhog predicts that we will have a longer winter than usual. It is hard to believe that summer is just around the corner.

First, I would like to take this opportunity to thank one of our Infectious Diseases Fellows in Training for her valuable contributions and service to the SOID. Dr. Adeline Koay is completing her term as a member of the SOID Executive Committee. She has been very active during her term and has written articles for the Fellows Column in the newsletter and has co-written the May 2018 Focus on Subspecialties article on “The pre-travel visit and post-travel infectious concerns”. She will also be serving as co-faculty with Dr. Kari Simonsen for an upcoming AAP Patient Care Online webinar regarding tickborne infections. She also has participated in numerous reviews of draft policy and book chapters providing a pediatric infectious diseases perspective. Adeline has really done an incredible job and we wish her the best of luck as she starts a new job.

Next, I would like to recognize SOID past Chair, Dr. Dennis Murray for his ongoing efforts to champion interprofessional telephone/internet consultation CPT codes that, as the title of the article states, may increase patient access and subspecialist tracking and productivity electronically and by telephone. You can read more on page 5.

There have been many opportunities for member participation within the SOID over the past few months including the call for nominations for the 2018 SOID Education Award, the open Training Fellow Liaison position and the call for applications for the 2018-19 S. Michael
Marcy Visiting Professor Program. Stay tuned in to the fall newsletter for updates on those items! A big thanks to Dr. Sheldon Kaplan who served as the S. Michael Marcy visiting professor on November 15-17, 2017 at Texas Tech University Health Science Center in Amarillo, Texas. And in this edition of the newsletter, please see the Travel Grant opportunity for ID fellows in training and resident members of the SOID on page 15.

As you are aware, this influenza season has been relatively severe with the influenza A H3N2 strain being the predominant strain circulating in the community. This strain is known to be associated with higher rates of complications and morbidity and mortality. Because of a mutation in the virus during manufacturing of the influenza vaccine, vaccine effectiveness to the influenza A H3N2 strain is decreased. There continues to be a lot of misconception and mistrust in the community about receiving influenza vaccine. This is true even among families whose normal healthy child contracts influenza and develops severe respiratory distress resulting in an admission to the PICU and the need for mechanical ventilation or who dies from the disease. Even though vaccine effectiveness varies from year to year, studies have shown that pediatric patients who receive an influenza vaccine have a reduced risk of laboratory-confirmed influenza-associated pediatric death. (Flannery B, et al. Influenza vaccine effectiveness against pediatric deaths: 2010-2014. Pediatrics 2017;139(5):e20164244). And, a study from Japan demonstrated that in adults with heart failure, those who received influenza vaccine had a 50% decreased risk of dying during influenza season and a 20% decreased risk of dying for the rest of the year. So even though the influenza vaccine is not perfect, it does work 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 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) to let us know how we can best serve your needs.

Best wishes for a wonderful Spring and Summer.

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

ID Training Fellows Column: Antibiotic Allergy Misdiagnosis

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

Adeline Koay MBBS MSc, FAAP
SOID Executive Committee Training Fellow Liaison, Johns Hopkins University, Baltimore, MD

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

The prevalence of drug allergies in children is 6-10%, based on parental report. The drugs most commonly involved are antibiotics and anti-epileptics, with beta lactams the most commonly implicated at 45-52%. True allergies are mediated by the adaptive immune system. Many reported allergies, however, instead represent non-allergic adverse reactions such as diarrhea, vomiting or maculopapular rash. As well, in young children, bacterial or viral infections often cause hives or maculopapular rash, which can be misinterpreted as an allergy if an antibiotic is being administered concomitantly. Similarly, other idiosyncratic reactions may be confused for allergy. One such example is when children with Epstein-Barr virus infection are given an aminopenicillin, which can induce an exanthem and may be misinterpreted as an allergic reaction.

Misdiagnosis of antibiotic allergy has important implications in clinical care, and can result in unnecessary use of broad-spectrum antibiotics. Patients with a penicillin allergy label, who may therefore receive alternative and/or broader spectrum drugs, have an

Continued on Page 3
increased risk of antibiotic-associated side effects, including longer hospital stays, increased rates of medication side effects, and increased rates of infection with *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE).\(^8,9\)

**Clinical Manifestations of Antibiotic Allergies**

Allergic reactions are commonly classified as either immediate (occurring < 1 hour after exposure) or non-immediate (≥ 1 hour, and commonly several days, after exposure), depending on when they occur after exposure to the drug. In nearly all cases, both types require pre-formed antibody to respond to a specific allergen, i.e. presensitization.

- Immediate reactions represent the classic Gell and Coombs IgE mediated type I reactions, and most commonly manifest with urticaria, angioedema, anaphylaxis, and anaphylactoid reactions.\(^10\)
- Non-immediate reactions, or delayed-type hypersensitivity reactions, usually result from cytokine release by activated T cell subsets, and manifest as maculopapular exanthems or non-immediate urticarial rashes. Less commonly, more serious reactions such as fixed drug eruption, serum sickness syndrome, Stevens-Johnson syndrome, or toxic epidermal necrolysis can occur.\(^11\)

Oftentimes, a child is labeled as “allergic” to a medication by their parent, without a pediatrician’s or other provider’s clinical assessment. In one study, 60-70% of penicillin users had a reaction within 24 hours of their first exposure to the medication, and the majority of these patients exhibited symptoms more consistent with drug toxicity rather than true allergy.\(^5\) It is important to counsel families regarding the difference between these clinical entities, as an adverse drug reaction does not constitute an absolute antibiotic restriction.

**Antibiotic Allergy Testing**

The gold standard for diagnosis of penicillin allergy is a 3-tier testing process, which involves a percutaneous skin test, followed by more sensitive intracutaneous testing, and ultimately an oral drug challenge.\(^12\) Skin testing only predicts rapid onset IgE-mediated allergic responses, while oral challenge also predicts non-immediate reactions. Oral drug challenge should always be performed in a medical setting with the immediate ability to treat anaphylaxis.\(^13\)

There is sometimes a reluctance from parents and providers to perform appropriate antibiotic allergy testing, as it can be a painful and time-intensive procedure. When children do undergo testing, few are confirmed to be truly allergic to the drug. In fact, a recent study of 100 children who were determined to be low-risk for severe allergy based on a questionnaire found that all 100 were negative for penicillin allergy after the 3-tier testing process.\(^14\) Once a patient is appropriately deemed non-allergic to a certain antibiotic, it is important to remove the allergy diagnosis from a patient’s medical record, thus facilitating the use of antibiotics that were previously thought to cause allergies.

Another recent study by Mill et al. demonstrated that graded oral provocation challenges are safe and accurate in confirming risk of skin-related reactions to amoxicillin, with a specificity of 100%, negative predictive value of 89%, and positive predictive value of 100%.\(^15\) History of a reaction occurring within 5 minutes of exposure was associated with immediate allergic reaction to the challenge, while non-immediate reactions were more commonly seen in patients with a history of allergic rash lasting longer than 7 days and parental history of drug allergy. Despite proven safe methods of testing for antibiotic allergies, less than 0.1% of patients with reported penicillin allergy undergo appropriate testing annually in the United States.\(^13\)

**Reducing the Burden of Antibiotic Allergy Misdiagnosis**

Appropriate allergy testing, followed by correction of the medical record and discussion with the family about the actual lack of an immune-mediated drug allergy are important actions that clinicians should perform. The downstream benefits may include reassurance to the patient and family regarding future medication use. As well, it can safely decrease broad spectrum antibiotic use, reduce the length of inpatient stay for hospitalized patients, decrease mortality rates, and reduce treatment costs.\(^16\) Evaluation for true antibiotic allergy using the methods outlined above is warranted for any patient carrying a diagnosis of antibiotic allergy. Obtaining a detailed history of a self-reported allergy allows for removal of an “allergy” label in up to 20% of hospitalized patients, and consultation with allergy specialists can facilitate cases where further testing may be required.\(^17\) Patients, families, and providers should understand the risks

*Continued on Page 4*
associated with carrying a diagnosis of antibiotic allergy, the proven safe methods of testing for antibiotic allergy, and the benefits of removing an antibiotic allergy label, when appropriate.

References:


The latest edition of the [AAP Academic and Subspecialty Advocacy Washington Report](#) is now available. The report details the important advocacy work that the Academy is engaging in and highlights issues of particular importance to medical and surgical subspecialty pediatricians. The report includes updates on AAP advocacy efforts to protect Medicaid, extend the Children’s Health Insurance Program, prevent gun violence, promote pediatric subspecialty workforce issues, increase funding for pediatric research, and improve drugs and medical devices for children, among many other issues.
Interprofessional Consultations: Ways to Increase Both Patient Access and Subspecialist Productivity Electronically and by Telephone

Dennis Murray, MD, FAAP, FIDSA
Immediate Past Chair, SOID
and
AAP Division of Health Care Finance

The AAP Committee on Coding and Nomenclature and Section on Infectious Diseases (SOID) have been advocating for the adoption of new Interprofessional Telephone/Internet Consultation CPT codes (99446-99449) since 2010 (See related AAP News article). These codes were approved by the CPT Editorial Panel and valued by the American Medical Association/ Specialty Society Relative Value Scale Update Committee (RUC) in 2012 – for implementation during the 2014 CPT/RBRVS cycle. The codes are:

- **99446** Interprofessional telephone/Internet assessment and management service provided by a consultative physician including a verbal and written report to the patient’s treating/requesting physician or other qualified health care professional; 5-10 minutes of medical consultative discussion and review
- **99447** Same as above; 11-20 minutes of medical consultative discussion and review
- **99448** Same as above; 21-30 minutes of medical consultative discussion and review
- **99449** Same as above; 31 minutes or more of medical consultative discussion and review

While the codes appeared in the CPT nomenclature, the Centers for Medicare and Medicaid Services (CMS) declined to publish the RUC valuation recommendations for the codes on the Medicare Resource-Based Relative Value Scale (RBRVS) physician fee schedule. Furthermore, CMS assigned the codes status indicator ‘B’ (Bundled), meaning that the service was considered bundled into other services for purposes of Medicare payment. An ‘A’ (Active) code status indicator would have made the codes separately billable under the Medicare program.

As champions of the codes, the Academy prioritized advocacy efforts with CMS to include the RUC-recommended values for the codes on RBRVS. While designated the Medicare physician fee schedule, most non-Medicare payers (including Medicaid) utilize RBRVS in setting their own fee schedules. As such, RBRVS is an important standard for pediatric payment.

AAP advocacy efforts continued for over three years – with no response from CMS. However, in November 2017, as part of the 2018 RBRVS final rule, CMS did publish the RUC-recommended values for codes 99446-99449, albeit still as ‘B’ (Bundled) status. This is an important distinction because subspecialists may now use these published values to document the time spent addressing these calls/internet contacts and may want to include them as part of their productivity tracking.

In September 2017, the AMA Digital Medicine Payment Advisory Group (DMPAG) developed two new CPT codes as part of the expansion of telehealth services for implementation on January 1, 2019:

- The **first code** will describe the work of a primary provider seeking the expertise and guidance of a subspecialist through an alternative model of care whereby the primary provider reviews the patient chart and fully represents the patient’s issues in lieu of the patient having a face to face visit with the subspecialist. The primary provider is documenting and securely transmitting the patient information electronically and then reviewing the subspecialist response electronically. This alternative model enables increased access to subspecialty care for patients who have access issues.

- The **second code** describes the work of a subspecialist providing expertise and guidance to a primary physician through an alternative model of care whereby the subspecialist needs to rely on the primary physician’s information in lieu of the patient having a face to face visit with the subspecialist. The subspecialist is documenting and securely transmitting their recommendations electronically to the primary physician. This alternative model enables increased access to subspecialty care for patients who have access issues.

It is important to note that the new subspecialist code only differs from the existing 99446-99449 codes in the following ways:

- Codes 99446-99449 require both verbal and written reports – while the new second code only requires a written report, which can be provided via an electronic health record

Continued on Page 6
• Codes 99446-99449 each include specific time increments, while the new second code only requires a 5-minute minimum threshold

The AMA DMPAG requested that the Academy take the lead on surveying the two new codes for valuation during the January 2018 RUC meeting. Members of SOID – as well as the Sections on Administration & Practice Management, Endocrinology, Pediatric Pulmonology & Sleep Medicine, Developmental & Behavioral Pediatrics, and Nephrology – were randomly selected to participate in the survey. Members of the American College of Physicians (ACP) participated in the survey, as well.

The RUC accepted the AAP and ACP valuation recommendations during its January 2018 meeting. RUC recommendations will be forwarded to CMS for inclusion on 2019 RBRVS (2019 RBRVS rule will be released mid-summer 2018). We are hopeful that CMS will publish RUC recommended values and assign status indicator ‘A’ (Active) for all 6 codes (99446-449 plus the 2 new codes on 2019 RBRVS). Watch for more information on use of these codes this fall in the AAP News Coding Corner.

For additional information, please contact Linda Walsh at lwalsh@aap.org.

---

**Pre-Travel Consultations to Reduce the Risk of Infections**

*Chris Anna Mink, MD, FAAP*

Voluntary Clinical Professor of Pediatrics, Harbor-UCLA Medical Center at the David Geffen School of Medicine

Travel to international destinations has grown in popularity in the past decade. In 2016, nearly 35 million U.S. residents traveled to a foreign destination, according to the National Travel and Tourism Office. People travel abroad for business, visiting friends and relatives (VFRs), humanitarian aid, education and just plain (or should that be plane?) fun.

The number of children traveling internationally is also increasing. In 2014, nearly 2.5 million children and adults with children ventured beyond U.S. borders. However, many children do not receive necessary pre-travel care. Only 51% of children, compared to 59% of adults, received pre-travel healthcare. The number was even lower, just 32%, for children who were VFRs, according to the GeoSentinel Surveillance Network, a global surveillance collaboration of the Centers for Disease Control and Prevention (CDC) and the International Society of Travel Medicine (ISTM).

Going abroad may expose travelers to unfamiliar pathogens or diseases controlled by vaccines in the U.S, such as measles. Upon returning home, travelers may bring non-endemic infections to their communities and even contribute to the spread of emerging infectious diseases, as seen with Ebola, pandemic influenza and Zika.

**Common infections** in travelers are diarrhea (enterotoxigenic E. coli is most common), respiratory infections (viral agents are the main culprits), systemic febrile illnesses and dermatologic disorders, such as insect bites and bacterial infections. Two of the most common vaccine-preventable diseases are influenza and hepatitis A.

**Pre-travel counseling** can mitigate some of the health risks for the individual traveler, as well as help prevent the spread of pathogens. Resources for travel advice are shown in Table 1.

Pediatric infectious disease specialists may be called upon for pre-travel care for children and teens, as well as adult family members. The consultation should include discussions about preventive measures for infectious, as well as non-infectious, maladies; though this article focuses on infection prevention.

**Pre-Travel Visit**

Ideally, pre-travel appointments should occur at least 4 to 6 weeks prior to departure. However, Hamer and Connor reported that only 36% of international travelers from the U.S. sought pre-travel medical advice and among those who did, 75% of the visits occurred within 28 days of their departure.5 Even with short-notice, a pre-travel consultation can be beneficial for the traveler.
Pre-Travel Consultations to Reduce the Risk of Infections

To assess the health risks of the trip, the characteristics of the traveler and the itinerary must be reviewed. Information needed about the traveler includes age, immunization status, underlying health status, allergies, current medications, special conditions (e.g., pregnancy, immunocompromise) and mobility (e.g., impaired mobility, crawling infants). For the itinerary, the travel season, all locations to be visited, the activities scheduled and the duration of the trip determine the potential exposures.

**Adventure travel**, such as mountain climbing, rafting or jungle backpacking, poses high risk for infections, trauma and other illnesses, such as altitude sickness. Adventure travelers may have exposure to contaminated water, extreme weather conditions and limited access to emergency care, dictating the need for additional preparations.

**VFRs** have an increased risk of acquiring infections for several reasons, including longer travel, greater likelihood of visiting remote areas and receiving less pre-travel medical care. Ericsson et al reported that only 16% of immigrant VFRs sought pre-travel care. In addition, VFRs often have greater immersion into local culture and cuisine, which may increase exposure to unsafe water and food. Infant and child VFRs are at even greater risk, as they are likely immune-naïve to infections endemic in their relatives’ homeland.

**Components of the Visit**

**Vaccinations**
All routine vaccinations, including influenza, should be up-to-date for age. For infants too young to be immunized, if possible, travel should be deferred or vaccines given on an accelerated schedule. Some vaccines may be given early for at-risk travelers. For example, measles vaccine may be administered to infants as young as 6 months if they are traveling to an endemic area.

Travel-specific vaccines are needed for certain destinations or activities, including yellow fever, typhoid, rabies, Japanese encephalitis and cholera. Vaxchora was recently licensed for use in adults in the U.S.). Documentation of yellow fever vaccination (or contraindication) may be required for entering endemic areas in South America and Africa.

**Malaria Prophylaxis**
Malaria prophylaxis should be chosen based upon drug resistance at the destination, as well as the traveler’s needs (e.g., child’s weight, drug adverse effects, ease of the regimen and cost). Information about epidemiology and malaria medications is available on the CDC travel website.

**Vector Protection**
Guidance about protection against arthropods should be provided to help decrease exposure to vector-borne infections such as Zika.

---

**Table 1. Select Resources for Pre-Travel Counseling**

<table>
<thead>
<tr>
<th>Resource</th>
<th>Source</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Travel website <a href="https://wwwnc.cdc.gov/travel">https://wwwnc.cdc.gov/travel</a></td>
<td>Centers for Disease Control And Prevention (CDC)</td>
<td>Up-to-date information about health risks and preventive measures for healthcare providers and for general public</td>
</tr>
<tr>
<td>Traveler Safety <a href="https://travel.state.gov/content/travel/en/international-travel.html">https://travel.state.gov/content/travel/en/international-travel.html</a></td>
<td>U.S. Department of State</td>
<td>Current data about safety risks, e.g. terrorist threats and civil unrest</td>
</tr>
<tr>
<td>International Society of Travel Medicine <a href="http://www.istm.org/">http://www.istm.org/</a></td>
<td>ISTM</td>
<td>Information for travel medicine professionals and a list of travel clinics.</td>
</tr>
</tbody>
</table>

---

Continued on Page 8
malaria and dengue, among others. Appropriate repellents (e.g. DEET and 20% picaridin) can be used on exposed skin for anyone older than 2 months. Permethrin should be applied to clothing and bed nets. When possible, travelers to infested areas should sleep in air conditioning with closed windows.¹

**Travelers' Diarrhea (TD)**

TD is the most common travel-related illness, occurring in 30-70% of travelers, and the most challenging to avoid.⁹ For infants, breastfeeding is safest. Travelers should be cautious with food and beverage choices and adhere to hand hygiene. This is especially difficult for children. Alcohol-based hand sanitizer is convenient and effective.

Prophylactic antibiotics are not routinely recommended.

**Medications**

Beside malaria prophylaxis, few immunocompetent travelers require preventive prescription medications.

Medications, with appropriate education about use, may be prescribed for treatment of select infections. The most common self-treatment medication is for TD and azithromycin is the antibiotic of choice for all ages. For some high-risk travelers (such as those with limited access to medical care), carry-along antibiotics may be prescribed in case symptoms of malaria or dysentery develop.⁹

**Sexual Health**

Review of safer sex practices, including condom use, should routinely be included in pre-travel counseling for all adolescents and adults.

**Health Insurance**

Many domestic insurance plans do not provide coverage for foreign travel, adventure activities or emergency medical evacuation. Purchasing additional insurance may be necessary, especially for high-risk travelers.

In summary, preparation, prevention and precautions can decrease the risk of illness for travelers, as well as decrease the risk of global spread of infectious diseases.

**References:**

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.

Despite an ACIP recommendation in 2006 for a two-dose mumps vaccination policy for both school-aged children (i.e., kindergarten through grade 12) and adults at high-risk (i.e., college students, health care workers, and international travelers), repeated mumps outbreaks have been reported in the US. These especially have been noted in intense-exposure settings where there is close, prolonged contact (e.g., universities and close-knit communities). The CDC has provided guidance on the use of a third dose of mumps virus-containing vaccine in specific target populations, such as individuals within a mumps outbreak. Nevertheless, the number of mumps cases reported in 2016 (6,369) and 2017 (5,629 preliminary as of December 31), are the highest reported numbers in over 10 years. A recent outbreak of mumps among a highly-vaccinated student population at the University of Iowa afforded an ideal opportunity to both evaluate the effectiveness of a third dose for outbreak control and assess waning immunity.

Increasing numbers of mumps cases were noted on campus during the 2015-2016 academic year. Of approximately 22,000 undergraduate students enrolled from July 2015 through May 2016, 98.1% had received at least two doses of a mumps virus-containing vaccine (university requirement since 2012) before the outbreak period. As a response to the outbreak, the university held eight mass vaccination clinics over 10 days targeting students <25 years of age. Fisher’s exact test was used to compare unadjusted attack rates according to dose status and years since receipt of the second MMR vaccine dose. A multivariable time-dependent Cox regression model evaluated vaccine effectiveness, according to dose status (three vs. two doses and two vs. no doses) after adjustment for the number of years since a second MMR dose.

Approximately a quarter (n=4,494) of the target student population received a third dose of MMR vaccine during the campaign. Vaccinations were initiated prior to the highest peak of the outbreak permitting a concurrent comparison of two doses versus three doses of MMR vaccine. Mumps was confirmed in 259 students. The attack rate was lower in students who received three doses than in peers who had received only two (6.7 vs. 14.5 cases per 1000 population, P<0.001). The vaccine effectiveness of the third dose vs. the second dose was 60.0% (95% CI, 38.4 to 74.0) at 7 days after vaccination. At 28 days post vaccination, receipt of a third MMR dose was associated with a 78.1% lower risk of mumps than receipt of a second dose (95% CI, 0.12 to 0.39). Vaccine effectiveness did not vary by student age. The vaccine effectiveness of two doses vs. no doses was lower among students with more distant receipt of the second vaccine dose. There was a stepwise increase in the risk of mumps with increased time since the second dose: attack rate of 1.6 cases per 1000 if second dose was administered within the 2 previous years, 3.9 cases per 1000 if administered within 3-12 years, 11.3 cases per 1000 if administered 13-15 years earlier, and 17.6 cases per 1000 if the vaccine was administered 16-23 years prior.

The investigators concluded that waning immunity likely contributed to the mumps outbreak in this highly vaccinated population and that the outbreak was mitigated with a third dose of MMR vaccine.

Reviewers Commentary:
This study demonstrated that a third dose of MMR vaccine can offer protection to fully vaccinated individuals (i.e., those with two doses of MMR vaccine) in an outbreak setting. The attack rate was lower among students who had received three doses than in those who had received only two doses (6.7 vs. 14.5 cases per 1000 population, respectively). Furthermore, among students who completed a 2-dose MMR series, an increasing risk of mumps relative to the number of years since the second dose was noted. Students who received their second MMR dose 13 or more years before the outbreak began had 9 to 14 times the risk of mumps as those who received the second dose more recently. One limitation to the findings of this observational study, however, relates to potential student receipt of a third dose on the basis of perceived risk. This would likely underestimate vaccine effectiveness. Additionally, some may have sought medical care in a setting other than the clinics sponsored by the university.

Continued on Page 10
It is important to note that the vaccine campaign was one effort among additional endeavors implemented to curb the outbreak: increased public health coordination between the university and local health departments, strong adherence to isolation recommendations, and heightened student awareness about the infection and the vaccine. While third dose administration of MMR vaccine is an effective response to localized outbreaks, efforts must continue to address the problem of mumps immunity. For example, the mumps vaccine strain (Jeryl Lynn strain) is genotypically distinct from current circulating strains. A better vaccine might be needed.

The CDC recently recommended that individuals previously vaccinated with two doses of a mumps virus-containing vaccine who are identified as being part of a group or population at increased risk for acquiring mumps because of an outbreak should receive a third dose of a mumps virus-containing vaccine to afford protection against mumps. Routine three-dose MMR vaccination regimen is not recommended.

References:

For more information on use of a third dose of MMR in an outbreak, see Dr. Harrison’s article, “ID Pearls and Other Gems: Four Reasons for More Outbreaks of Measles and Mumps than Rubella” on page 16 of this newsletter.


Reviewed by: Jane Gould, MD, FAAP, Associate Professor of Pediatrics, Drexel University College of Medicine, Hospital Epidemiologist, Attending Physician, Section of Infectious Diseases, St. Christopher’s Hospital for Children, Philadelphia, PA.

*Pseudomonas aeruginosa* has become a common healthcare associated infection (HAI) in children and has become increasingly antibiotic resistant. Multidrug resistant (MDR) infections are more difficult to treat than drug susceptible infections. According to the CDC, 51,000 *P. aeruginosa* HAIs occur in adults and children, 6000 of which are MDR, leading to 400 deaths each year. Most studies of *P. aeruginosa* infections in pediatrics have occurred in patients with cystic fibrosis (CF); however, other pediatric populations are also at high risk, such as those with immunocompromising conditions, those with urinary tract indwelling hardware and those in ICU settings, especially burn patients. The study by Logan et al is the first to assess national antimicrobial trends in *P. aeruginosa* infections in children, from both inpatient and outpatient settings, excluding those with CF and infants.

Logan et al conducted a retrospective analysis using the Surveillance Network (TSN) Database-USA from 1999-2012, which obtains data from clinical microbiology laboratories serving approximately 300 US hospitals from 9 Census Bureau regional divisions selected to be representative by geography, hospital size and patient population. The laboratory data submitted were interpreted using Clinical Laboratory Standards Institute (CLSI) criteria and includes specimen source, healthcare setting, geographical location, patient age and sex, as well as date and results of the susceptibility testing of all agents within 5 antibiotic classes. MDR was defined using CDC criteria as non-susceptibility to agents in at least 3 of the following 5 classes: cephalosporins, β-lactam/β-lactamase inhibitor combination, carbapenems, fluoroquinolones and aminoglycosides. A total of 77,349 isolates tested against 5 antibiotic classes found that 20% (15,653) were MDR, 11% were carbapenem resistant (CR) and 8% were both MDR and CR. During 1999-2012, the proportion of MDR increased from 15.4% to 26% and the proportion of CR increased from 9.4% to 20%. These increases were statistically significant. Multivariate analysis revealed that MDR and CR were more prevalent in the intensive care setting, among children 13-17 years of age, in respiratory specimens and from the West North Central region of the U.S. The prevalence of MDR *P. aeruginosa* was highest in long
term care settings, but there were not enough isolates from this setting for the authors to draw a strong conclusion.

**Reviewer’s Commentary:**
One of the study limitations was that the investigators were unable to differentiate rising rates of MDR and CR colonization from clinical infection. Colonization is not only a pre-requisite to infection, it also represents a failure of infection control practices both in the hospital and in outpatient settings such as long-term care facilities. Robust antimicrobial stewardship programs in these varied healthcare settings and a regional infection control response will be vital to curtailing the spread of MDR organisms. These efforts require facility administrative support as well as local public health department programming to improve inter-facility communication.


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

**Objective:** To derive and test new and existing risk prediction models for pneumonia and serious bacterial infections in acutely ill febrile children.

**Methodology:** Children < 16 years of age with documented or history of fever (>38oC) and without a history of primary immunodeficiency presenting to the emergency department of a single British children’s hospital were prospectively evaluated between November 2010 and April 2012. In addition to vital signs and a detailed physical examination, CBC and differential counts, urinalysis, blood cultures and chest radiographs were obtained on all subjects; other testing was performed at the discretion of the treating provider. The targets for prediction were pneumonia and serious bacterial infection (bacteremia, meningitis, UTI, osteomyelitis, septic arthritis and probable serious infection). A parsimonious logistic regression model was derived in a forward-stepwise fashion using the c statistic as the tuning metric. The model of Nijman, et. al.1 was validated using the entire patient dataset; for validation, the threshold probabilities of pneumonia or SBI, were set at <0.05 and >0.20 to rule out or rule in the diagnosis, respectively.

**Results:** 1101 of 1872 (58.8%) eligible patients were recruited for this study. The median age was 2.4 years (IQR; 0.9, 5.7 years) and the a priori outcome probabilities were 0.142 and 0.098 for pneumonia and SBI, respectively. For more than 95% of subjects, C-reactive protein, procalcitonin, resistin and NGAL were obtained. The statistically significant predictors (adjusted ORs) in the newly derived model included CRP > 30 (1.01; 95% CI: 1.003,1.018), respiratory rate (1.048; 95% CI: 1.021,1.076), procalcitonin concentration (1.189, 95% CI: 1.079, 1.310), and normal air entry (0.092; 95% CI: 0.046, 0.182) for pneumonia, and CRP > 30 (1.012, 95% CI: 1.005,1.018 ), CRP < 30(1.046, 95% CI: 1.011, 1.081) and procalcitonin concentration (1.183, 95% CI: 1.074, 1.303) for other SBIs.

The model of Nijman, et. al. was updated by recalculating the coefficients using the new data set and was extended with the inclusion of CRP and resistin (extended model). At a predicted probability of .05, the updated model produced actual posterior probabilities of .11 and .03 for pneumonia and SBI, respectively; at a predicted probability of .20, the updated model produced actual posterior probabilities of .69 and .56 for pneumonia and SBI, respectively. Results from the extended model of Nijman, et. al were slightly better.

**Conclusions:** The authors conclude that these models discriminated well between pneumonia and other SBIs in the emergency room.

**Reviewer’s Commentary:**
This study is among the first of a new generation of clinical studies that analyzes large databases using computer algorithms often associated with artificial intelligence. Logistic regression, used in this study, and other machine learning algorithms come with their own nomenclature and problems. This paper illustrates one of those problems. A good predictive model balances the ying/yang errors of machine learning: bias and variance. In basic terms, bias is the intrinsic oversimplification of a model. An example of a model with high bias is the use of a line to describe a curvilinear dataset. While the line may yield some degree of prediction, a curving model, such as a polynomial curve, may better describe the data. Bias is overcome with the correct selection of a learning algorithm. In the case of the present study, a parsimonious logistic regression model seems appropriate. Variance, on the other hand, is a measure of the over sensitization of a model to small fluctuations in data, i.e. noise in the data. Also known as overfitting, models with high variance may
perfectly predict the response of interest in the training dataset but may fail horribly in predicting outcomes in new data. Overfitting can be minimized by using a separate dataset for validation of the model or by cross validation within the training set. Irwin, et. al. attempted to validate an existing model with a new dataset; this was commendable and potentially useful. With the new dataset, the authors noted that the reported model1 “discriminated well between pneumonia and no SBI but not as well between SBI and no SBI”. The authors then “updated” the coefficients of the variables in the existing model and extended the updated model to include procalcitonin and resistin. As noted above, these models performed well on the dataset. That is expected since the authors essentially retrained the existing model on new data and then created a totally new model by adding two new features, producing two newly derived but non-validated models. The real conclusion of this paper is in the supplementary material and shows that the area under a receiver operating curve for the model of Nijman, et. Al. went from 0.854 (95% CI: .810,.899) on the training set to 0.755 (95% CI: .708,.801) on the validation set; the associated c statistics, which estimate the probability that the model will place a randomly selected subject from the test set into the correct group was .85 for pneumonia vs no SBI and .76 for SBI vs. no SBI. As a rule of thumb for diagnostic purposes, both the c statistic and AUC should exceed .90. These data suggest that the previously reported model is discriminative but probably not clinically useful. Validation of the two new models is required before an assessment of clinical utility can be made.

Reference:

---

**Acute Uncomplicated Appendicitis: Medical or Surgical Options: Which to Choose?**

**Infectious Disease:**

*Alexandra Vinci MD FAAP, Pediatric Hospitalist*

The Children’s Medical Center at NYU Winthrop Hospital (avinvi@nyuwinthrop.org)

*Leonard Krilov, MD, FAAP, Chairman, Department of Pediatrics*

Chief, Pediatric Infectious Disease, NYU Winthrop and Professor of Pediatrics
SUNY Stony Brook School of Medicine (lkrilov@nyuwinthrop.org)

**Surgery:**

*Rivfka Shenoy, MD, General Surgery Resident, UCLA Health System*

(RivfkaShenoy@mednet.ucla.edu)

*Steven L. Lee, MD, FACS, FAAP, Professor of Clinical Surgery and Pediatrics*

David Geffen School of Medicine at UCLA, Chief of Pediatric Surgery
Division of Pediatric Surgery, UCLA and Harbor-UCLA
(StevenLee@mednet.ucla.edu)

Acute appendicitis remains the leading cause of all inpatient surgical procedures in the pediatric population. Although most cases are treated with surgical removal, successful resolution of infection with antibiotic therapy alone has been demonstrated in patients with early, uncomplicated (i.e. non-perforated) appendicitis. The debate over antibiotic treatment as opposed to immediate appendectomy in the setting of acute uncomplicated appendicitis – although not a novel concept - is ongoing. Pros and cons to both approaches are illustrated in the literature and individual randomized controlled trials often conflict with one another. Because of this, each case of acute appendicitis should be evaluated on an individual basis to determine the best course of action.

8 year-old girl presents with abdominal pain, nausea, and vomiting for 12 hours. Pain was periumbilical and now in RLQ. She is tender to palpation and it hurts her to jump. WBC count is 13,000 and US shows a 9 mm, dilated and hyperemic appendix. No appendicolith or free fluid is noted.

Continued on Page 13
Is this patient a candidate for non-operative management with antibiotics alone?

This patient fits the criteria for early, uncomplicated appendicitis: inflammation of the appendix without concurrent abscess, phlegmon, perforation, gangrene, visualized appendicolith or peritonitis. Therefore, both surgeon and infectious disease (ID) specialist agree that she is a candidate for treatment with broad spectrum antibiotics alone. Many prospective studies examining the role of non-operative management have strict inclusion criteria: pain < 48 hours, WBC count < 18,000, appendix diameter < 1.1cm and absence of appendicolith and rupture. In clinical practice, only about one-third of patients will meet such stringent criteria. However, for the majority of patients who meet the definition for early, uncomplicated appendicitis, it is appropriate to attempt non-operative management (NOM).

What is the antibiotic course?

Both ID specialist and pediatric surgeon agree that patients should initially be treated with broad-spectrum IV antibiotics which include ceftriaxone and metronidazole, meropenem or piperacillin-tazobactam. Parenteral antibiotics should be continued until the patient is afebrile, pain is controlled, and they are able to tolerate clear liquids on a consistent basis. Once this is achieved, it is appropriate to switch the patient to oral antibiotics to complete a 7-10 day course. Amoxicillin-clavulanate and metronidazole are generally the oral antibiotics of choice for pediatric surgeons while our ID colleagues feel that just amoxicillin-clavulanate is sufficient in most cases. Adult regimens of ciprofloxacin and metronidazole may be considered for adolescent patients. It is important to note that patients who undergo laparoscopic appendectomy only require preoperative antibiotics; no post-operative antibiotics are needed for acute, uncomplicated appendicitis managed with laparoscopic surgery.

What is the anticipated success rate and recurrence?

Various studies have been conducted to identify the rates of initial success and of recurrence. Initial success rate of NOM in pediatric studies of uncomplicated disease range from 87%-95%, which is notably higher than in the adult population where the initial success rate is only 60%. The one-year recurrence rate is estimated at 15-20%. The long-term recurrence rate is not known, although one study from Japan identified a recurrence rate of 28.6% at a 4 year follow-up. Those who failed conservative treatment and needed appendectomy at a later date had a medical course without serious complications (similar to surgical management of appendicitis). However, it is important to note that pediatric studies have been conducted on a notably smaller scale then their adult counterparts and are mainly prospective observational studies and not randomized, controlled trials. Further evidence obtained from larger, randomized trials would be helpful in validating the high rate of antibiotic treatment success.

Other described benefits of the non-operative approach include a decreased rate of major (perforations, postsurgical adhesions) and minor (incisional wound infections) complications, faster return to normal activity, avoidance of potential dangers of general anesthesia and less use of analgesics (low to moderate quality evidence). However, patients treated with antibiotics alone demonstrate a higher rate of hospital readmission, with approximately 25% requiring an appendectomy within one year of initial presentation seen in adult patients. The one-year recurrence rate is estimated at 15-20%. The long-term recurrence rate is not known, although one study from Japan identified a recurrence rate of 28.6% at a 4 year follow-up. Those who failed conservative treatment and needed appendectomy at a later date had a medical course without serious complications (similar to surgical management of appendicitis). However, it is important to note that pediatric studies have been conducted on a notably smaller scale than their adult counterparts and are mainly prospective observational studies and not randomized, controlled trials. Further evidence obtained from larger, randomized trials would be helpful in validating the high rate of antibiotic treatment success.

Slightly different scenario...8 year old girl presents with abdominal pain, nausea, and vomiting for 12 hours. Pain was periumbilical and now in RLQ. She has mild tenderness to palpation and WBC count is 13,000. US does not visualize the appendix.

Is it reasonable to start antibiotics in this patient?

Both ID specialist and pediatric surgeon firmly agree that it is not reasonable to initiate antibiotics in this patient without a diagnosis of appendicitis. In most cases, visualization of the inflamed appendix confirms the diagnosis. Therefore, if history, physical exam, lab studies, and ultrasound are insufficient in diagnosing appendicitis, further imaging with contrast tomography or magnetic resonance imaging should be considered. Some studies demonstrate that reduced-radiation CT scans (which deliver a mean effective radiation dose 78% less than standard-dose CT) are not inferior in sensitivity and specificity to standard CT. Radiologic confirmation is not always required to make the diagnosis of appendicitis. If a surgeon makes the diagnosis of appendicitis based on history, exam and laboratory data, then it is reasonable to start IV antibiotics and discuss treatment options (surgery vs. NOM).

From an ID specialist standpoint, in situations of low clinical suspicion for appendicitis, patients may be discharged with close clinical follow-up or admitted for rehydration and serial abdominal exams. Initiating broad spectrum antibiotics without a definitive diagnosis...
undoubtedly contributes to the ever-growing dilemma of emerging multi-drug resistant organisms. In addition, if the patient improves after antibiotic administration, it will be difficult to discern if they did indeed have appendicitis, if they had another intra-abdominal infection, or simply a resolving acute gastroenteritis.

Slightly different scenario...8 year old girl presents with abdominal pain, nausea, and vomiting for 48 hours. Pain was periumbilical and now in RLQ. She has tenderness to palpation and WBC count is 13,000 and US shows a 12 mm appendix with appendicolith.

**Is it reasonable to attempt non-operative management in this patient?**

Several factors exclude this patient from conservative management with antibiotics alone: abdominal pain for 48 hours, the presence of an appendicolith and an appendix diameter greater than 1.1 cm on imaging. “Early” symptoms of appendicitis do not extend beyond 48 hours and findings on imaging studies prohibit one from labeling this case “uncomplicated.” This patient has a higher risk of having complicated appendicitis. Recent studies that have looked at broadening the inclusion criteria for NOM to include duration of symptoms ≤ 5 days, presence of appendicolith, and no restriction on appendiceal diameter or WBC count had an initial failure rate of 30%, due mostly to gangrenous appendicitis or contained perforation. In particular, patients with an appendicolith had a 50% initial failure rate11. Therefore, this patient should undergo immediate surgical appendectomy with appropriate pre-surgical antibiotic prophylaxis. Of note, patients for whom initial NOM was attempted had no difference in morbidity and length of stay compared to patients who underwent immediately laparoscopic appendectomy11. Thus, it is not necessarily contraindicated to attempt a trial of antibiotics and other patient factors may need to be considered.

The above cases demonstrate that careful consideration must occur on a case by case basis regarding the immediate surgical treatment versus NOM with antibiotics alone for acute appendicitis. Both pediatric ID physicians and pediatric surgeons use similar decision-making pillars (history and physical examination, laboratory and imaging data) to decide between immediate surgical treatment vs. antibiotic trial for acute appendicitis. Antibiotics alone can be a successful method of treating uncomplicated acute appendicitis as a majority of patient cases avoid surgery and its associated complications. However, there is no universal consensus on the absolute criteria that distinguishes complicated from uncomplicated appendicitis. It is generally accepted that the presence of abscess, rupture, appendicolith and/or peritonitis exclude patients from being categorized as “uncomplicated.” Immediate surgical removal likely aids in antibiotic stewardship efforts while providing the only definitive treatment for acute appendicitis. The above cases demonstrate that consideration of individual patient factors is of utmost importance when making a decision to operate or to simply treat with antibiotics.

**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

**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. Diagnosis and Management of Bone and Joint Infections (IDSA/PIDS)
3. Clinical Guidelines for Diagnosis and Antiviral Management of Seasonal and Pandemic Influenza in Adults and Children (IDSA)
4. 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
5. Clinical Practice Guidelines Practice Guidelines for Outpatient Parenteral Antimicrobial Therapy (IDSA)

**From the ACIP Meeting of October 2017 and February 2018**

The slide sets and minutes from these meetings are available [here](#). The next ACIP meeting is scheduled for June 20-21, 2018.

**FYI: Accessing the SOID Website**

The easiest way to access the SOID website is to save it as a favorite (Internet Explorer) or bookmark it (Firefox) on your computer. Go to the SOID webpage at: [https://www.aap.org/en-us/about-the-aap/Committees-Councils-Sections/Section-on-infectious-diseases/Pages/default.aspx](https://www.aap.org/en-us/about-the-aap/Committees-Councils-Sections/Section-on-infectious-diseases/Pages/default.aspx) For Internet Explorer, click on favorites and then add to favorites.

**SOID Travel Grant Awards**

The Section is pleased to offer NCE travel grants for the 2018 NCE to residents with an interest in infectious diseases or ID fellows in training who are AAP/SOID members. Complete the [application](#) and submit it by May 11, 2018 to [lrutt@aap.org](mailto:lrutt@aap.org)

**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](http://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.
ID Pearls and Other Gems: Four Reasons for More Outbreaks of Measles and Mumps than Rubella

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.

One Measles-Mumps-Rubella (MMR) dose at 12-15 months of age was considered adequate when the combined vaccine was introduced (Figure 1). This convenient one-dose schedule was modified after the 1990s adolescent/college measles outbreaks to add a second dose given anytime, more than a month after the first dose, but usually at 4-6 years old. Recently, a third MMR dose has been used to restrict disease during mumps outbreaks.1,2 Why do outbreaks still occur, with mumps and measles outbreaks occurring more frequently than with rubella? Why would two doses not be sufficient to protect against mumps?

Figure 1. Measles Cases and MMR Dose Recommendations 1968-2017.
Light Blue Inset Reflects % with 1 vs. 2 MMR Doses after 1995. *

Adapted from figure in presentation (Current Mumps Vaccination Recommendations and Epidemiology in the United States) by Mona Marin MD, Division of Viral Diseases National Center for Immunization and Respiratory Diseases CDC at ACIP Meeting Atlanta, GA, February 23, 2017. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2017-02/mumps-02-marin.pdf

Dr. Harrison’s institution received grant funds for research for which he is an investigator from Alios, Allergan, Cubist, GalxsoSmithKline, Merck, Pfizer, and Rida Gene Diagnostics. He received one honorarium and travel reimbursement for presentation of pneumococcal seroepidemiology research results.

Continued on Page 17
1. Stringency of herd immunity requirements for measles plus loss of herd immunity in sub-herds. The degree of contagion and the proportion of the population that is immune determine the number of secondary infections produced by a typical infectious disease. The basic reproductive rate (number of secondary cases caused by each new imported case into a totally susceptible population) is the R0 (pronounced R naught). Effective herd immunity reduces the R0 to <1, i.e. less than one secondary case, so ongoing outbreaks should not occur. In an unprotected population, the R0 for measles is 12-18, for mumps it is 4-7 and for rubella it is 5-7.3 Because of its higher R0, more of the herd needs to be immune (>95%) to attain herd immunity against measles than mumps or rubella. (Table 1)

In pockets where vaccine refusers cluster, outbreaks are more likely and impact special populations including children under age one year and those who are immunocompromised. And if a contagious person (often in prodrome or not yet clinically diagnosed) travels widely, there is more chance that a vulnerable sub-herd will be exposed. For MMR, the vulnerable population includes children <1 year old who are not yet able to be immunized.

With a secondary attack rate of 12-18 new cases per index case, it is not difficult to see why multiple geographically divergent outbreaks can occur from a single imported, but mobile measles case. Consequently, measles outbreaks make some sense. One would; however, postulate that mumps’ lower R0 should make outbreaks less. So, why so many mumps outbreaks?

2. Variable host response to differing MMR components. Primary vaccine failure (no host response to the first dose of vaccine) is estimated at 2-5% for measles, up to 5% for mumps, and 1% for rubella.4,5 The second MMR dose results in seroconversion of most primary failure patients so that the expected vulnerable population after a second dose should be <2% for measles and mumps while being near zero for rubella after two doses.6

Initial seroconversion with later breakthrough has not been thought to be the major issue for measles vaccine. Measles seroconversion seem to protect against secondary laboratory-confirmed measles (first dose ~92% effective in up to school age and two doses ~95% 10 years post vaccine. i.e. in young teens).6 No estimate of efficacy vs rubella was possible in a 2013 Cochrane report because there were so few reported secondary rubella cases, but protection seems to mirror initial seroconversion rates (~98%).6 Compared to measles and rubella, mumps vaccine estimates of post-seroconversion protection have been lower (first Jeryl-Lynn mumps vaccine dose 64-66%, and two doses 83-88%).

This raises the question of waning immunity. The dogma on measles and rubella protection is that “breakthrough cases” are due almost entirely to primary vaccine failure, not waning immunity7 (Table 1). While waning rubella antibody levels were reported for preteens prior to their second dose, >99% have rubella antibody after the second dose7; most reports indicate > 90% persistence and high avidity (avidity measures how tightly antibody binds to its target) rubella antibody at 20 years post rubella vaccine8,9 (Table 1) This persistence parallels the protection against rubella disease (see prior paragraph).

Lower initial titers plus waning immunity and lower avidity antibody occur with mumps vaccine and also with mumps immunity from wild type infection.8,10 As a result, waning immunity seems important for mumps but not measles or rubella. Hence, there is hope that a third dose during outbreaks will be beneficial.2

---

**Table 1. Characteristics Affecting Potential Vaccine Protectiveness for MMR**

<table>
<thead>
<tr>
<th></th>
<th>R0</th>
<th>% of Population Being Immune to Produce Herd Immunity</th>
<th>% Avidity of Vaccine Induced Antibody</th>
<th>% Antibody 20 Years Post Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Protective Low Negative</td>
</tr>
<tr>
<td>Measles</td>
<td>12-18</td>
<td>&gt;95%</td>
<td>~70%</td>
<td>82 13 5</td>
</tr>
<tr>
<td>Mumps</td>
<td>4-7</td>
<td>88-92%</td>
<td>~20%</td>
<td>40 34 26</td>
</tr>
<tr>
<td>Rubella</td>
<td>5-7</td>
<td>82-85%</td>
<td>~80%</td>
<td>93 7 0</td>
</tr>
</tbody>
</table>

---

Continued from Page 16

Continued on Page 18
3. **Subtle changes in circulating wild type viruses compared to the strains used in the vaccines.** Circulating strains of the viruses may not match those in the vaccines. There are at least four amino acid differences between a common wild-type measles strain and the highly attenuated Edmonston vaccine strain.\(^{11}\) Rubella also has differing wild type genotypes and within a genotype there can be differences compared to the RA27/3 US vaccine strain.\(^{12}\) But mumps has at least 25 variants that differ from Jeryl-Lynn strain.\(^{13}\)

This could mean that even if the MMR induces good and durable antibody responses to the mumps vaccine strain, the protection might not be as good against variant circulating strains. The good news is that available data so far suggest that circulating mumps strains continue to be neutralized *in vitro* by vaccine-induced antibody.

4. **The intensity and duration of exposure may cause breakthrough disease.** Most mumps outbreaks include secondary vaccine failures and occur in high population density situations e.g., college campuses. So, mumps exposures are likely more intense and more frequent, two factors that can enhance transmission. High inoculum exposures on multiple occasions have a better chance to cause infection in the face of two-dose, albeit waning, mumps antibody. The CDC states that the current 2-dose schedule is sufficient for mumps control in the general population, but outbreaks can occur in well-vaccinated populations in specific settings.

**Take home message.** The message to share with families is that MMR is a good vaccine and has dramatically reduced the prevalence of disease. The best protection depends on making sure we reach the goal of >95% MMR uptake to maintain herd immunity, and limiting as much as possible sub-herds (geographical clusters of unimmunized) that lose herd immunity. Further, getting two doses on time is very important to reduce windows of vulnerability (primary vaccine failures). Mumps vaccine has the lowest rate of long term protection even with two doses and has the most secondary vaccine failures (although still >80% protection). But if a mumps outbreak occurs, a third dose may be needed and could be recommended by local or state public health groups.

**For more information on use of a third dose of MMR in an outbreak, see Dr. Alter’s review of the NEJM article on page 9 of this newsletter.**

**References:**


ID Pearls and Other Gems: Four Reasons for More Outbreaks . . .  Continued from Page 18


---

**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](http://www2.aap.org/sections/infectdis/policy.cfm)

I. AAP

A. **Recommended Childhood and Adolescent Immunization Schedules: United States, 2018**. *Pediatrics* 2018; 41(3).

1. Changes to the schedule include simplifying (i.e., using bullets instead of sentences) and updates to the footnotes on:
   - Hepatitis B. More information on the timing of the birth dose for infants with a birth weight of <2000 g who are born to HBsAg-negative mothers has been added.
   - *Haemophilus influenzae* type b. MenHibrix (Hib-MenCY) has been removed. The vaccine is no longer commercially available and all remaining doses have expired.
   - Influenza. Wording indicates that LAIV is not recommended for the 2017–2018 influenza season.
   - Meningococcal vaccines. Only MenACWY vaccines are discussed in footnote #11. MenB vaccines are discussed in a separate footnote (#12).
   - Polio vaccines. Updated wording provides guidance for children who have received oral polio vaccine as part of their series.
   - MMR vaccines. Guidance is provided in regard to use of a third dose of a mumps-containing vaccine during a mumps outbreak.

2. Changes were also made to Figure 2 (Catch-up immunization schedule for persons aged 4 months through 18 years who start late or who are more than 1 month behind)

3. The rotavirus vaccine row has been modified to include the maximum ages for the first and last doses of the series.

4. The polio vaccine rows clarify the catch-up schedule for people 4 years or older.

To learn more about other changes made to the Schedule, please see the AAP Policy Statement: the *AAP News* article and the CDC MMWR.

B. **Infection Prevention and Control in Pediatric Ambulatory Settings**, *Pediatrics* 2017, 140 (5).


2. Policies for infection control should be updated every 2 years.

3. In general, standards for infection prevention and control are the same in the ambulatory and the hospital settings.

4. Section on Cystic Fibrosis patients was added.

Continued on Page 20
5. A 1-page summary of policies at the end of the statement should be reviewed by every health caregiver who has contact with patients and specific sections can be reviewed in detail and followed.

C. **Infectious Diseases Associated with Organized Sports and Outbreak Control.** *Pediatrics* 2017;140:1-25.
   1. Table 2 summarizes pathogens, transmission, diagnosis, treatment and management of outbreaks.
   2. Table 3 summarizes pathogen with regards to return to competition guidelines.

D. **Elimination of Perinatal Hepatitis B: Providing the First Vaccine Dose Within 24 Hours of Birth.** *Pediatrics* 2017;140:1-5.
   1. ~1000 new cases of perinatal Hepatitis B infection are identified annually in US.
   2. Chronic Hepatitis B infection occurs in up to 90% of infants infected at birth or in the first year of life.
   3. Hepatitis B vaccine alone is 75-95% effective in preventing perinatal Hepatitis B transmission when given 24 hrs. of birth.
   4. Hepatitis B vaccine and HBIG and completion of Hep. B immunization series decreases perinatal infection rates to ~1%.
   5. Recommendations also included for treatment and follow up of infants born to HBsAg positive or unknown status mothers.

E. **Practical Approaches to Optimize Adolescent Immunization.** *Pediatrics* 2017;139:e1-16.

II. **MMWR**


B. **Recommendation of the Advisory Committee on Immunization Practices for Use of a Third Dose of Mumps Virus-Containing Vaccine in Persons at Increased Risk for Mumps During an Outbreak.** *MMWR* January 12, 2018/67(1);33-38.
   1. 3rd dose of MMR recommended to help improve protection for persons at increased risk of mumps in an outbreak.
   2. In 1977, ACIP recommended 1 dose of mumps vaccine for children >12 mos.
   3. In 1989, due to multiple measles outbreaks in the 1980’s, the ACIP recommended 2 doses of MMR at ages 12-15 mos. and 4-6 yrs.
   4. In 2006, increased mumps cases were noted affecting populations with 2 doses of vaccine thought to be due to waning immunity.

C. **Recommendations of the Advisory Committee on Immunization Practices for Use of Herpes Zoster Vaccines.** *MMWR* January 26, 2018/67(3);103-108.
   1. October 25, 2017, ACIP recommended Zoster Vaccine Recombinant (RZV), a 2-dose, subunit vaccine containing a recombinant glycoprotein and a novel adjuvant (Shingrix, GlaxoSmithKline) for use in immunocompetent adults aged >50 yrs.
   2. Zoster Vaccine Live (ZVL) (Zostervax, Merck and Co.) a 1- dose live attenuated strain of VZV was recommended in 2008 after licensure.
   3. Data comparisons on efficacy, duration of protection and side effects between ZLV and RZV were evaluated.
   4. RZV is recommended for the prevention of Herpes Zoster in immunocompetent adults who previously received zoster vaccine live (ZVL).
   5. RZV is preferred over ZVL for prevention of Herpes Zoster and related complications.
   6. Full rationale and summary of findings that lead to these recommendations can be found in the report.

III. **IDSA**

A. **2017 Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea.** *Clin Inf Dis* 2017;65:e45-e80.
   2. Guidelines focus on the clinical presentation of acute and persistent diarrhea with emphasis on infectious etiologies in the U.S.
   3. Recommendations are given for specific diagnoses and management.
New Policy/Guidelines  Continued from Page 20

IV. HIV Guidelines
Complete 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. New are updated recommendations on ARV management of infants born to women with HIV which includes ARV prophylaxis, empiric HIV therapy to those newborns at risk for HIV acquisition, and HIV therapy to newborns with confirmed HIV infection.
   3. Table included to provide overview and guidance about specific antiretroviral management and ARV dosing recommendations.

B. 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. Updates are based on panel review of all recent scientific studies available and should be checked monthly on website.

C. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV.
   2. Newly added section on when to start ART.
   3. New safety and clinical trial data added.
   4. Emphasis on NOT using monotherapy.

   1. Updated October 18, 2017.
   2. Sections on Candida, bacterial enteric infections, hepatitis B virus, Pneumocystis pneumonia and Toxoplasma gondii encephalitis updated.
SOID Leadership Roster

THE SECTION ON INFECTIOUS DISEASES • EXECUTIVE COMMITTEE

Tina Tan, MD, FAAP
Ann & Robert H. Lurie
Children’s Hospital of Chicago
Northwestern University
Feinberg School of Medicine
Chicago, IL
Telephone: (312) 227-4080
EM: titan@luriechildrens.org

Susan Coffin, MD, FAAP
Children’s Hospital of Philadelphia
Philadelphia, PA
Phone: (215) 590-2096
EM: coffin@email.chop.edu

Deborah Faccenda, MD, FAAP
Pennridge Pediatric Associates
Sellersville, PA
Phone: (215) 257-2727
EM: drfaccenda@gmail.com

Lilly Immergluck, MD, FAAP
Morehouse School of Medicine, Emory University
Pediatric Infectious Disease Specialist
with Children’s Healthcare of Atlanta (CHOA)
Atlanta, GA
Telephone: (616) 822-9385
EM: limmerg@emory.edu and limmergluck@gmail.com

Robert Frenck, MD, FAAP
Cincinnati Children’s Hospital
Medical Center
Cincinnati, OH
Telephone: (513) 636-4463
EM: robert.frenck@cchmc.org

ID TRAINING FELLOW LIAISONS
Sophie Katz, MD, FAAP
Vanderbilt University Medical Center
Nashville, TN
Telephone: (615) 835-8744
EM: sophie.e.katz@vanderbilt.edu

Adeline Koay, MBBS, MSc, FAAP
John Hopkins University
Baltimore, MD
Telephone: (410) 614-3917
EM: adelinokoay@jhmi.edu

NC&E PLANNING GROUP REPRESENTATIVE
Anne Rowley, MD FAAP
EM: a-rowley@northwestern.edu

NOMINATIONS CHAIRPERSON
Kari Simonsen, MD, FAAP
EM: kasimosens@unmc.edu

RBRVS CHAIRPERSON
Margaret Ikeda, MD, FAAP
EM: ocikeda26@hotmail.com

WEBSITE CONTENT DIRECTOR
Lilly Immergluck, MD FAAP
EM: limmerg@emory.edu and limmergluck@gmail.com

NEWSLETTER EDITORS
Jane M. Carnazzo, MD FAAP
EM: jmcarnazzo@cox.net
Jennifer S. Read, MD, MS, MPH, DTM&H, FAAP, FPIDS, FIDSA
EM: read@post.harvard.edu

NEWSLETTER EDITORIAL BOARD
Sherman Alter, MD, FAAP
EM: sherman.alter@wright.edu
Stephen Aronoff, MD, FAAP
EM: Stephen.Aronoff@tuhs.temple.edu
Jane Gould, MD FAAP
EM: Jane.Gould@DrexelMed.edu
Christopher J. Harrison MD, FAAP
EM: cjharrison@cmh.edu
Sophie Katz, MD, FAAP
EM: sophie.e.katz@vanderbilt.edu
Adeline Koay, MBBS, MSc
EM: adelinokoay@jhmi.edu
Katie Richardson, MD, FAAP
EM: kmrichardson@cmh.edu
Andrea Sperduto, MD, FAAP
EM: sperdua@ccf.org

EDUCATION/PROGRAM CHAIRPERSON
Ken Zangwill, MD, FAAP
EM: kzangwill@labiomed.org

EDUCATION SUBCOMMITTEE
Sherman Alter, MD, FAAP
EM: sherman.alter@wright.edu
Jane M. Carnazzo, MD FAAP
EM: jmcarzanno@cox.net
Robert Frenck, MD FAAP
EM: Robert.Frenck@cchmc.org
Lilly Immergluck, MD FAAP
EM: limmerg@emory.edu and limmergluck@gmail.com
Sabah Kalyoussef, MD, FAAP
EM: sbenz61@gmail.com
J. Michael Klatte, MD, FAAP
EM: James.KlatteMD@baystatehealth.org
Grace Lee, MD, MSCE, FAAP
EM: gracelee430@gmail.com
Edgar K. Marcuse, MD, MPH, FPIDS, FAAP
EM: emarcuse@uw.edu
Leena Mithal, MD, FAAP
EM: LMithal@luriechildrens.org
Angela L. Myers MD, MPH, FAAP
EM: amyers@cmh.edu
Jennifer Read, MD, MS, MPH, DTM&H, FAAP, FPIDS, FIDSA
EM: read@post.harvard.edu
Katie Richardson
EM: kmrichardson@cmh.edu
Kari Simonsen, MD, FAAP
EM: kasimosens@unmc.edu
Jennifer Vodzak, MD, FAAP
EM: jvodzak@cmh.edu
James Wilde, MD, FAAP
EM: jwilde@gru.edu
S. Elizabeth Williams, MD MPH, FAAP
EM: elizabeth.williams@vanderbilt.edu

AAP STAFF
Suzanne Kirkwood, MS
Manager, Section of Infectious Diseases
Phone: (800) 433-9016, ext. 6648
Fax: (847) 434-8000
EM: skirkwood@aap.org

Mark A. Krajecki
Prepress Production Specialist