Greetings, SOID Members! Hope everyone has been enjoying the relatively mild winter that we are having and has taken time to be outdoors and enjoy the sunshine. It is hard to believe that summer is just around the corner.

First, I would like to take this opportunity to thank several of our infectious diseases fellows in training for their valuable contributions and service to the SOID. Dr. Ishminder Kaur is completing her term as a member of the SOID Executive Committee and Dr. Emily Souder is completing her term as a member of the SOID Education Subcommittee. Together they wrote an article regarding *Staphylococcus aureus* decolonization that will be published in May, 2017 *AAP News* Focus on Subspecialties column and another regarding “Career Paths in Pediatric Infectious Diseases” (see page 6) for the Section on Pediatric Trainees newsletter. Both have participated in numerous reviews of draft policy and book chapters. In addition, Dr. Kaur has developed a survey for past fellow liaisons to identify ways to further enhance this role and had the opportunity to attend a Committee on Infectious Diseases (COID) meeting. Finally, Dr. Souder is working with Dr. Elizabeth Barnett to develop another in a series of ID-related online courses, “Challenging Cases: Dengue, Chikungunya and Zika Virus Infections” which should be released by the end of June, 2017. The fellows have done an incredible job and we wish them the best of luck as they start their new jobs.

There have been many opportunities for member participation within the SOID over the past few months including the call for nominations for the 2017 Education Award, the open Training Fellow Liaison positions and the call for applications for the 2017-18 S. Michael Marcy Visiting Professor Program. Stay tuned in to the fall newsletter for updates on those items! A big thanks to Dr. Sarah Long who served as the visiting professor on January 23-24, 2017 at Crozer Chester Medical Center in Chester, Pennsylvania.

*Continued on Page 2*
Finally, thank you to the 2017 PREP ID Planning Group Co-Chairs, Lilly Immergluck and Lorry Rubin and members, Lara Danziger-Isakov, Bob Frenck, Angela Myers and Debra Palazzi for their time and commitment in planning the *2017 PREP ID: A Comprehensive Update of Pediatric Infectious Diseases and Antimicrobial Therapy* live course which is co-sponsored by the SOID and the Pediatric Infectious Diseases Society. The course will be held on **July 27-30, 2017** in Dallas, Texas and offers a shorter, more interactive and improved format. We are very excited to be partnering with the editors of the *Nelson’s Pediatric Antimicrobial Therapy* book regarding course content in that area. The course will assist in preparations for the initial or recertification ID subspecialty exams, and will provide an update on important pediatric infectious diseases information for general pediatricians, family physicians, nurses, nurse practitioners, physician assistants and pharmacists. This is shaping up to be a great course so please help us spread the word to your fellows and colleagues!

An issue that is of critical importance and one that we as pediatricians need to continue to be strong advocates for is the effectiveness and safety of vaccines. Given the current administration’s anti-vaccine attitude and their support for the formation of a committee on Vaccine Safety and Scientific Integrity that would readdress a possible association between vaccines and autism, as well as other discredited claims, it is imperative that we remain strong advocates and serve as a credible educational resource to the community on the importance of vaccines in maintaining the health of our patients. The attitude of this political administration threatens to destroy the significant progress that the U.S. has made in protecting our children from the morbidity and mortality caused by vaccine-preventable diseases. As new issues continue to arise, this is an important time to advocate for your patients. The AAP has resources regarding communication with parents, case studies on vaccine hesitancy and a vaccine social media toolkit available to members.

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*

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### Join the AAP Mentorship Program

Mentorship is one of the most important tools for professional development and has been linked to greater productivity, career advancement, and professional satisfaction. The AAP recognizes that mentorship is critical in helping to nurture and grow our future leaders and that a mentorship program is a key opportunity to engage new and existing members. The AAP Mentorship Program seeks to establish mentoring relationships between trainees/early career physicians and practicing AAP member physicians. [Click here](#) for more information and to join the program.

*Please note:* Mentors are asked to commit at least one full year. However, the program offers opportunities for short-term “flash” mentoring. Mentors/mentees will be asked to set regular phone meetings to discuss mentee goals, objectives, and progress. Mentors/mentees should also answer all communications in a timely manner.
ID Training Fellows Column -
The Future of Pediatric Infectious Diseases:
How do we Avoid the Void?

Ishminder Kaur, MD, FAAP1, Wei Li Koay, MD, FAAP2, Emily Souder, MD, FAAP2,
1St. Christopher’s Hospital for Children, Philadelphia, PA, 2Johns Hopkins University, Baltimore, MD

Overall, 87% of offered fellowship positions were filled in the 2017 National Resident Matching Program (NRMP®) Specialties Matching Service® appointment year (2016 match year).1 In the same year, only 62% of pediatric infectious diseases (ID) programs’ and 80% of adult ID training programs’ fellowship positions were filled.1 The near 40% unfilled rate for pediatric ID fellowship positions at 22 US programs at the end of the 2016 match contrasts with the rising fellowship applications among several other subspecialties.1 In a 2015 pediatric ID workforce survey, 20% of the respondents reported plans to decrease or stop pediatric ID practice within the next 5 years.2 The authors of this survey estimated that an annual replacement of 60 pediatric ID physicians would be required to maintain current levels of ‘pediatric ID coverage’.2 However, this estimated number would only provide replacement for the current attrition of the workforce, and does not take into account the expansion of the field and the potential need for more pediatric ID physicians. Amidst growing concerns about the pediatric ID workforce, the number of trainees enrolled in a three-year pediatric ID fellowship has not seen an increase since the year 2000, despite an increase in the number of fellowship positions offered.1,3

Timing of Career Choice
The critical question in designing any intervention to a problem is defining the target population. More often than not, the medical community assumes that fellowship decisions are made during residency. But is that the case? When it comes to choosing a career after graduating from residency, there is evidence that many residents develop an early interest in a specific field. In a national survey of 590 internal medicine residents (105 programs), 44% reported developing an interest in their chosen field in medical school and 21% reported the interest began prior to medical school.4 When specifically looking at the resident cohort who chose ID as a subspecialty, the number rose to 72% and 24%, respectively, highlighting the potential effect of early exposure to a field on future career decisions.4

Factors that Affect Post-Residency Career Choice
There are multiple factors that affect career choice and fellowship decisions for medical students and residents. A 2007 survey of pediatric residents in all US and Canadian training programs (n=8290) revealed that almost half of residents planned to pursue fellowship training after residency, with males and international medical school graduates (IMGs) being more likely to apply to a fellowship program.5 Interest in a specific disease or patient population favored the intent to pursue fellowship training, while the desire for structured work hours and lifestyle favored a general pediatrics career.5 Higher educational debt has also been associated with a lower likelihood of choosing fellowship training post-residency.6 Unfortunately, many of these factors are not easily amendable. Targeting modifiable factors that focus on early exposure to ID, such as medical school curricula, subspecialty rotations and mentorship programs, may be more effective than current efforts in promoting the field.

Role of medical school education and research opportunities
Limited data suggest that the design of teaching curricula in undergraduate and graduate medical education may affect career choice. Bonura et al found that residents who chose to specialize in ID were more likely to describe their medical school ID curriculum as being case- and laboratory-based, with the use of patient encounters, in contrast to a lecture-based structure with a focus on memorization reported by those who chose other subspecialties.1 Residents pursuing ID were also more likely to have a balance of basic science faculty and ID clinical faculty teaching the course as opposed to a higher percentage of basic science faculty for non-ID graduating residents.4 In addition to curriculum, participation in other educational opportunities such as research may influence an individual’s career path. A longitudinal study of medical students found that those who engaged in surgical research projects during their first year were more likely to retain an interest in a surgical career.7

Role of subspecialty rotations
The effect of subspecialty electives during medical school and residency on career choice has also been explored. A survey of graduated medical students who took a radiology elective during their second year of medical school found that 16% overall and 77% of those

Continued on Page 4
who chose a career in radiology reported the elective influenced their specialty choice. Another survey of rheumatology fellows found that 35% identified a rheumatology rotation during residency as being the most important factor in their specialty choice. According to Bonura et al, residents who chose ID as a career were also more likely to have completed an ID rotation compared with those who chose other career fields.

Role of mentors in career decisions

There is increasing evidence that mentorship plays a crucial role in shaping an individual’s career choice. A majority of survey respondents in varied fields (surgery, nephrology and pediatric dermatology) note mentorship as an important influence on the decision to pursue their respective careers. Mentees often make career decisions that align with their mentors’ area of interest. In a national survey of internal medicine residents, 80% of those who applied or planned to apply to ID fellowship (n=42) identified a mentor in ID, with one-third having established the relationship during medical school. It is difficult to ascertain from these studies if the mentors truly influenced the career choice of the mentees, or the mentees simply sought out mentors in their field of interest. However, a national survey of graduating pediatric residents showed that those with a subspecialist mentor had higher odds of having a subspecialty career goal compared with those with a generalist mentor, which held true even for residents who preferred primary care at the start of residency.

Current activities to promote the field of ID among applicants

Leading ID organizations recognize the challenges in recruiting young clinicians and researchers into the field of ID and have launched several programs and initiatives to address the problem. Table 1 provides a summary of some of these activities.

<table>
<thead>
<tr>
<th>Sponsor Organization</th>
<th>Program/ Initiative</th>
<th>Brief Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDSA (Infectious Diseases Society of America), through its Education and Research Foundation</td>
<td>IDWeek Mentorship Program</td>
<td>This program provides opportunities for mentorship and networking through one-on-one interactions between leaders in the field and trainees during IDWeek.</td>
</tr>
<tr>
<td></td>
<td>Infectious Diseases Interest Group (IDIG)</td>
<td>Launched in Fall 2016 to further trainee education and promote medical student interest in ID by awarding grants to interested medical schools to help support new/existing IDIG.</td>
</tr>
<tr>
<td></td>
<td>Medical Scholars Program</td>
<td>Launched in 2002, this program awards scholarships to medical students to support clinical or research activities with mentorship by an IDSA member.</td>
</tr>
<tr>
<td>HIVMA (HIV Medicine Association)</td>
<td>HIVMA Medical Student Program</td>
<td>The program provides scholarships to medical students interested in ID to support a longitudinal HIV-related research project with mentorship.</td>
</tr>
<tr>
<td>PIDS (Pediatric Infectious Diseases Society)</td>
<td>Brochure: Caring for Children Worldwide: Careers in Pediatric Infectious Diseases</td>
<td>This brochure describes the mission of PIDS, outlines career opportunities in the field of ID, and contains excerpts from leaders in the field.</td>
</tr>
<tr>
<td></td>
<td>Promotional videos</td>
<td>Series of videos discussing PIDS members and their career choices.</td>
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ID Training Fellows Column - The Future of Pediatric Infectious Diseases: . . . Continued from Page 4

### AAP and SOID

| **Visiting Professor Program** | This program provides support for a pediatric ID physician to visit an institution where there is no or limited access to a pediatric ID specialist. |
| **Travel grants** | Travel grants are provided to residents and training fellows to attend the AAP National Convention and Exhibition. |
| **Webpage: A Career in Pediatric ID, Considering a Fellowship?** | A webpage maintained by the SOID with links to articles promoting the field of pediatric ID by SOID Training Fellow Liaisons and other helpful resources. |

### AAP, PIDS and SOID

| **Pediatric Infectious Disease workforce survey** | The goal of the survey was to obtain information to assist in workforce planning in the field of pediatric ID. |

### New Concerns and Future Directions

While the collective ID community continues to grapple with the dwindling applications for ID fellowship positions, there is some early evidence that positive change may already be occurring. Adult ID saw an increase in the number of filled fellowship positions from 65% in 2015 to 80% in the 2016 NRMP match.\(^1\)\(^15\) It is difficult to know if this change is a direct result of the IDSA's efforts to promote ID and whether it will be sustained. Nonetheless, the trend is encouraging and reinforces the need for expansion of similar efforts in pediatric ID.

The current political environment also has the potential to affect the existing applicant pool. About one-third of the pediatric ID fellowship positions were filled by non-US IMGs in the 2016 NRMP\(^8\) match.\(^1\) The ID community must continue its efforts to recruit the brightest to ID, regardless of the applicant’s country of origin.\(^16\)

Moving forward, there is need for continued research to demonstrate the value of ID physicians.\(^17\) We all must do our part in promoting the field that we are so passionate about and continue to engage medical students and residents, be effective mentors and participate in or help create activities to promote ID, so we can strive to “avoid the void”.

### References


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ID Training Fellows Column - The Future of Pediatric Infectious Diseases: . . . Continued from Page 5


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**Anticipating and Managing Infectious Complications of Biologic Response Modifiers in Infants and Children**

*H. Dele Davies, MD, FAAP, FPIDS*

*Professor of Pediatrics and Public Health, University of Nebraska Medical Center; Member, AAP Committee on Infectious Diseases*

**What are biological response modifiers (BRMs)?**

BRMs are substances that dampen or stimulate the host immune system. The focus of this review is immune-dampening BRMs. Such BRMs target cytokines such as tumor necrosis factor-alpha (TNF-α); interleukin (IL) 6, 12, and 23; the receptors for IL1-alpha (IL1A) and IL 1-beta (IL1B); and other molecules. They are generally used in combination with other immunosuppressive agents, such as methotrexate and corticosteroids, or alone to treat conditions such as juvenile idiopathic arthritis, psoriatic arthritis, or inflammatory bowel disease (Table 1)1.

**What are the infectious risks of using BRMs?**

Children being treated with these immune-dampening BRMs are generally at increased risk of infection with or reactivation of infection with mycobacteria (*Mycobacterium tuberculosis* and nontuberculous mycobacteria), viruses (e.g., *Herpes simplex* virus, *Varicella zoster* virus, Epstein-Barr virus, hepatitis B virus), and fungi (e.g., *Histoplasma* sp., *Coccidioides immitis*)1.

**When should use of BRMs be considered and for whom?**

All patients with a newly diagnosed rheumatologic or immune-mediated condition should be considered as current or future candidates for a BRM and should be screened for potential opportunistic infections at the time of diagnosis, before any immunosuppressive agent is started. There should be a careful determination of infectious risk through a detailed history (including exposure, residence, and travel and immunization history) and selected baseline screening test results. Caution should be exhibited in prescribing BRMs to children who are being treated for chronic infections, those with a history of recurrent infections, or those with conditions (including HIV infection) that predispose them to opportunistic infections1. It is recommended that an infectious diseases specialist helps guide management, to ensure that all risks are assessed and appropriate screening tests are performed before treatment, and to ensure that appropriate monitoring occurs during and after treatment.

*Continued on Page 7*
Anticipating and Managing Infectious Complications . . . Continued from Page 6

What infectious risks should be considered during use of BRMs?
The risks associated with potential opportunistic infections that are endemic in the area of residence (eg, histoplasmosis, coccidioidomycoses, etc) should be considered before starting a BRM (Table 2). In particular, there needs to be determination of previous exposure to the infectious agent and the associated risk of reactivation or infection during treatment with the BRM1. Once a decision is made to treat with a BRM, close monitoring will be required, ideally in conjunction with an infectious diseases specialist. The risk of tuberculosis warrants special consideration (Table 2).

How should suspected infections be managed during treatment with BRMs?
In general, if the child develops symptoms suggestive of an opportunistic infection, there should be immediate discontinuation of the BRM while the infection etiology is sought, along with appropriate empiric management of the infection and resolution of the clinical findings. Serum neutrophil counts should be monitored regularly (weekly) in patients receiving rituximab due to the risk of associated neutropenia 2,3. Table 2 summarizes general considerations for suggested screening/immunizations and infectious management before, during, and after BRM initiation.

Summary
While BRMs are important agents for effective management of patients with a variety of autoimmune/inflammatory conditions, there is an associated increased risk of certain serious infections during and following treatment, particularly mycobacterial, fungal and viral infections. Anticipatory guidance and monitoring is important to reduce the risk of occurrence or of negative outcomes if complications do occur.

Table 1. FDA-Approved Biologic Response Modifiers and Indications*

<table>
<thead>
<tr>
<th>Generic Name (Year(s) FDA Approved for Indications)</th>
<th>Trade Name</th>
<th>Mechanism of Action</th>
<th>Usual Route, Half-Life</th>
<th>FDA-Approved Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab (1999, 2009)</td>
<td>Remicade⁴</td>
<td>TNF inhibitor (anti-TNF-α chimeric monoclonal IgG1κ antibody)</td>
<td>IV, 7.5–9.5 days</td>
<td>Crohn’s disease, rheumatoid arthritis, plaque psoriasis, psoriatic arthritis, ankylosing spondylitis, ulcerative colitis</td>
</tr>
<tr>
<td>Etanercept (1998)</td>
<td>Enbrel⁵</td>
<td>TNF inhibitor (soluble TNF-α receptor fusion protein)</td>
<td>SQ, 70–132 h</td>
<td>Juvenile idiopathic arthritis, rheumatoid arthritis, plaque psoriasis, psoriatic arthritis, ankylosing spondylitis</td>
</tr>
<tr>
<td>Adalimumab (2002)</td>
<td>Humira⁶</td>
<td>TNF inhibitor (Anti-TNF-α humanized monoclonal IgG1 antibody)</td>
<td>SQ, 10–20 days</td>
<td>Juvenile idiopathic arthritis, rheumatoid arthritis, plaque psoriasis, psoriatic arthritis, ankylosing spondylitis, Crohn disease</td>
</tr>
<tr>
<td>Golimumab (2009)</td>
<td>Simponi⁷</td>
<td>TNF inhibitor (Anti-TNF-α IgG1κ antibody)</td>
<td>SQ, 7–20 days</td>
<td>Rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis</td>
</tr>
<tr>
<td>Certolizumab pegol (2009)</td>
<td>Cimzia⁸</td>
<td>TNF inhibitor (PEGylated human Fab antigen binding)</td>
<td>SQ, 14 days</td>
<td>Rheumatoid arthritis, Crohn disease</td>
</tr>
</tbody>
</table>

Continued on Page 8
### Anticipating and Managing Infectious Complications . . .

<table>
<thead>
<tr>
<th>Drug</th>
<th>Approval Year(s)</th>
<th>Mechanism of Action</th>
<th>Route</th>
<th>Duration</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abatacept</td>
<td>2005, 2009</td>
<td>Anti-CTLA4 selective T cell co-stimulation modulator protein; (blocks TNF, IL-2 and interferon–γ production)</td>
<td>IV or SQ, 8–25 days</td>
<td>Juvenile idiopathic arthritis, [rheumatoid arthritis]</td>
<td></td>
</tr>
<tr>
<td>Anakinra</td>
<td>2001</td>
<td>Orencia Anti-CTLA4 selective T cell co-stimulation modulator protein</td>
<td>SQ, 4–6 h</td>
<td>[Rheumatoid arthritis]</td>
<td></td>
</tr>
<tr>
<td>Rituximab</td>
<td>2006</td>
<td>Rituxan Anti-CD20 therapy</td>
<td>IV, 14–62 days</td>
<td>[Rheumatoid arthritis, non-Hodgkin lymphoma]</td>
<td></td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>2010</td>
<td>Actemra Anti-IL6 humanized monoclonal antibody</td>
<td>IV, 8–14 days</td>
<td>[Rheumatoid arthritis]</td>
<td></td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>2013</td>
<td>Stelara Anti-IL12 and IL23 humanized monoclonal antibody</td>
<td>SQ, 20–24 days</td>
<td>[Psoriatic arthritis, plaque psoriasis]</td>
<td></td>
</tr>
<tr>
<td>Canakinumab</td>
<td>2009 2013</td>
<td>Ilaris Anti-IL1B human monoclonal antibody</td>
<td>SQ, 26 days</td>
<td>CAPS, [Juvenile idiopathic arthritis]</td>
<td></td>
</tr>
<tr>
<td>Natalizumab</td>
<td>2008, 2013</td>
<td>Tysabri Humanized anti integrin alpha 4 subunit monoclonal antibody (reduces leukocyte adhesion and transmigration)</td>
<td>IV, 11 days</td>
<td>[Crohn disease multiple sclerosis]</td>
<td></td>
</tr>
<tr>
<td>Belimumab</td>
<td>2011</td>
<td>Benlysta Human IgG1λ monoclonal antibody against soluble human B lymphocyte stimulator protein</td>
<td>IV, 19 days</td>
<td>[Systemic lupus erythematosus]</td>
<td></td>
</tr>
<tr>
<td>Riloncept</td>
<td>2008, Orphan Drug</td>
<td>Arcalyst IL1 receptor fusion protein</td>
<td>SQ, 8.6 days</td>
<td>CAPS</td>
<td></td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>2012</td>
<td>Xeljanz Small molecule protein kinase [inhibitor] of JAK-3 and JAK 1</td>
<td>Oral, 3 h</td>
<td>[Rheumatoid arthritis]</td>
<td></td>
</tr>
</tbody>
</table>

IV indicates intravenous; SQ, subcutaneous; CAPS, cryopyrin-associated periodic syndromes (consisting of familial cold autoinflammatory syndrome and Muckle-Wells syndrome).
#FDA-approved indication: for underlined conditions, safety and efficacy have been established in children <18 years; for bracketed indications, safety and efficacy have only been shown in adults. Infliximab, etanercept, and adalimumab have been used off-label for scleritis, but none are FDA-approved for this condition.

* Reprinted from reference 1 with permission from the American Academy of Pediatrics.

| Thorough history | ■ Document prior vaccinations, antibody testing when indicated (routine antibody testing not recommended for varicella) |
|                 | ■ Query about possible exposure and epidemiologic risk factors for histoplasmosis and coccidioidomycosis |
|                 | ■ Query about history of recurrent HSV |
|                 | ■ Consider serologic testing for Epstein-Barr virus |
|                 | ■ Screen for past hepatitis B infection with HbSAb, HbcAb (total and IgM), and quantitative HbSAb, and liver function tests (LFTs) and determine need for vaccine |

| Routine immunizations | ■ Follow current AAP, CDC, and American Academy of Family Physician guidelines.19 |
|                       | ■ Give recommended vaccines, inactivated, or subunit vaccines 2 weeks before initiation of BRM |
|                       | ■ Consider safety of giving live vaccine; if appropriate, give 4 weeks before initiating BRM |

| Tuberculosis screening and management | ■ Test for latent tuberculosis and manage based on result (see reference20 for algorithm) |

<table>
<thead>
<tr>
<th>Suggested Screening/Immunizations and Infectious Management After BRM Started*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine immunizations</td>
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<tr>
<td></td>
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</table>

| Immunizing immunocompetent household contacts (before or during treatment)? | ■ Follow AAP guidelines for immunizing household contacts of immunocompromised patients21 |

* Reprinted from reference 1 with permission from the American Academy of Pediatrics.

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Anticipating and Managing Infectious Complications . . . Continued from Page 9

| Risk of hepatitis B Reactivation (Chronic, occult, resolved) | ■ Monitor LFTs, HBsAg, HBeAg, and HBV DNA every 1–3 months, depending on underlying HBV infection, for at least 6 months after termination of the BRM |
| Risk of listeriosis | ■ Avoid unpasteurized milk and milk products, uncooked meats22 |
| Febrile or serious respiratory illness during BRM therapy | ■ Consider stopping BRM and actively search for infections including bacterial, mycobacterial (TB and non-tuberculous), and opportunistic infections including EBV, VZV, HSV, fungal (histoplasmosis and coccidioidomycosis), Pneumocystis depending on clinical scenario. |
| Suspected VZV or HSV infection during BRM therapy | ■ Stop BRM |
| ■ Confirm by combination of clinical, serologic, and PCR from skin lesions (ie, vesicles or papules) |
| ■ Start acyclovir or valacyclovir therapy pending confirmation of diagnosis. |

**Suggested Screening/Immunizations After BRM Stopped***

| Routine immunizations | ■ May still receive routine inactivated, polysaccharide, recombinant, or subunit vaccines* |
| Timing of giving live vaccines after stoppage of BRM ± other immuno-suppressives? | Consult infectious diseases specialist |

* These are suggestions only. Each situation should be guided by clinical scenario and the help of an infectious diseases consultant may be sought.

& If on rituximab, may not respond.

& Modified from reference 1; with permission from the American Academy of Pediatrics.

References

Anticipating and Managing Infectious Complications . . . Continued from Page 10


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: 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.

Retropharyngeal (RPA) and parapharyngeal (PPA) abscesses are common infections seen by pediatric infectious diseases physicians. There is some evidence that the incidence of these infections may be increasing in the U.S. Patients with these infections can quickly develop life-threatening complications such as airway obstruction, necrotizing fasciitis, mediastinitis and sepsis. The need for early surgical drainage is debatable. Some studies have suggested that patients treated with intravenous antibiotics without surgical interventions have similar outcomes compared with those with early surgical intervention with intravenous antibiotics. The authors of this manuscript conducted a national level retrospective study from 2003 to 2012 using the Kids Inpatient Database (KID). They examined the epidemiology and demographic characteristics of U.S. pediatric patients with these infections and also investigated whether early surgical drainage affected outcomes.

KID currently consists of all payer inpatient admissions data from 44 states for patients ≤ 20 years old. This study used International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) codes for either a primary or secondary diagnosis for RPA or PPA. Demographic and clinical information including surgical intervention, total charges adjusted to 2009 dollars, primary payer status and median household income were included. Results demonstrated an increase in hospital discharge RPA incidence from 2003 to 2012 (2.98-4.10 per 100,000, respectively) occurring in all age subgroups and in both sexes. The incidence of PPA increased from 2003 to 2006, peaking at 1.49 per 100,000 and plateauing thereafter. Incidences for RPA and PPA were highest in children less than 5 years old and for males in all age groups (1.63:1 for RPA and 1.47:1 for PPA). No statistical differences were seen in racial/ethnic distribution. Winter and spring (December through May) seasonality was observed for both infections, suggesting a potential pathogenic role for antecedent respiratory viral infections. Surgical drainage was performed in 46.7% of those with RPAs and 58.1% of those with PPA. This is consistent with other studies that have concluded that medical management alone is often insufficient. Most often surgical intervention occurred on either the day of admission or the next calendar day in 70% of RPA and PPA cases. The remaining 30% of patients with surgical intervention occurred on the second day or later (for lack of improvement, progression of disease or delay in diagnosis) representing approximately 14% of RPA cases and 17% of PPA cases. The proportion of PPA cases with surgical intervention did not change from 2003 to 2012, but the proportion of RPA cases with surgical intervention decreased from 49.5% in 2003 to 44.3% in 2012. For PPA, 59% were initially managed medically with 29% later undergoing surgical drainage, and, for RPA patients, approximately 67% were initially managed medically with 21% later undergoing surgical drainage. The median length of stay declined for both RPA and PPA (4.26 to 3.90 days vs. 4.25 to 3.58 days respectively) and was 1 day longer for PPA and RPA with surgical drainage compared to those with either condition who did not have surgery. The median charges per hospitalization were approximately double for cases that included surgery compared with those who received medical management alone ($21,777 vs $11,473 for RPA and $20,416 vs $10,689 for PPA, respectively). The proportions of hospital discharges covered by Medicaid for either entity increased from 2003 to 2012.

Reviewer’s Commentary:
This study provides additional evidence for an increasing national incidence of both infections and that most of these infections are successfully treated medically without surgical intervention. Unfortunately, the study was not able to provide information on the microbiology of these infections and whether this too is changing over time.


Reviewed by: Stephen C. Aronoff, MD FAAP, Temple University School of Medicine.
This study was undertaken to determine if ZMapp, a mixture of 3 monoclonal antibodies directed against the surface antigens of Ebola virus, would reduce the 28-day mortality rate in PCR-positive patients enrolled in endemic countries and the U.S. An adaptive, randomized, controlled study was used. This design permitted the incorporation of new, as yet undiscovered, therapies into both arms of the ZMapp protocol while preserving data. Because of this design, the uncertainty regarding duration of therapy and the potential need to take frequent “peeks” at the data, a Bayesian statistical approach was taken. A posterior probability ≥ 97.5 was required to establish efficacy. Patients were stratified according to estimated baseline inoculum (≤22 PCR cycles vs > 22 cycles) and location. ZMapp was administered to the treatment group in a dosage of 50 mg/kg three times, every third day. No placebo was given. The primary outcome was mortality on day 28 of illness.

Patients were enrolled until the end of the epidemic. Of 72 patients enrolled, 71 completed the protocol: the two groups were comparable except for a slight predominance of women and children in the experimental arm. 13/36 (37%) control and 8/35 (22%) experimental patients died; the Bayesian estimate of relative risk was 0.62 (0.29-1.24) and the posterior probability of ZMapp superiority was 0.912. The authors conclude that ZMapp therapy may be beneficial, although efficacy did not reach the probability established a priori.

Reviewer’s Commentary:
James Lind, who studied the effect of lemon juice on scurvy in British sailors, is credited with performing the first controlled clinical trial in 1747. Placebo controls were introduced in 1863, alternate day assignment to groups appeared in the late 19th century and the multi-centered, randomized, placebo controlled trial appeared in the mid-20th century. This study design has become the gold standard for establishing clinical efficacy for new drugs. In recent years, the high costs in time and money, the limited ability to generalize results from narrowly-defined experimental samples, and the inflexibility of the classical clinical trial have led to newer designs. Pragmatic studies introduced flexibility in recruitment, intervention, follow-up and data analysis. Adaptive studies permit scheduled, interim data analyses along with changes in the study protocol. This study was designed to accommodate unplanned protocol changes. While this is somewhat consistent with adaptive studies (changes are usually planned), the scheme to preserve the data collected prior to protocol change was novel. By applying a Bayesian methodology, the authors were able to: (i) evaluate the data at unplanned times, such as when a new treatment became available or the epidemic ended, without incurring a “statistical penalty”; (ii) continue to use any data acquired prior to protocol changes via the prior distribution required in Bayesian analysis, and (iii) calculate the exact probability that the mortality rates in the treatment and control groups were different along with estimates of the rate ratios and rate differences with associated credible intervals. As adaptive studies become more common, it is reasonable to expect that investigators will avail themselves of Bayesian techniques to analyze the results and draw inferences.


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


**Clostridium difficile** is the most frequent cause of nosocomial diarrhea in the developed world. The extensive utilization (and abuse) of antibiotics, among other risk factors, are thought to be paramount in causing *C. difficile* infections (CDIs). Although antimicrobial treatment of primary CDI is often successful, up to 35% of patients will have recurrent infections. This study evaluated the use of
two human monoclonal antibodies, bezlotoxumab (BMAB) and actoxumab (AMAB), in preventing recurrent CDI. BMAB binds to \textit{C. difficile} toxin, thereby inhibiting the binding of toxin B to host intestinal cells and neutralizing its effects. AMAB is presumed to block toxin A activity by the same mechanism. Both must be used in conjunction with antibiotics to treat recurrent CDI.

The paper described two double-blind, randomized, placebo-controlled phase 3 trials, in 30 countries involving 2655 adults receiving standard-of-care antibiotics (metronidazole, vancomycin, or fidaxomicin for 10-14 days) for primary or recurrent CDI. Study subjects received either a single weight-based intravenous infusion of BMAB, BMAB plus AMAB, or placebo. The long half-life of the monoclonal antibodies (19 hours) supported the single-dose treatment. The primary endpoint was recurrent CDI (new episode after initial cure) within 12 weeks after infusion in the modified intention-to-treat population.

BMAB therapy resulted in initial clinical cure rates similar to those seen in the placebo group. However, BMAB achieved a significant benefit over placebo in preventing recurrent CDI. In the first study (MODIFY I), recurrent infection in the BMAB group was 17% versus 28% in the placebo group (P<0.001). In the second study (MODIFY II), the rates of recurrent CDI were again significantly lower in the BMAB group versus placebo, 17% versus 26% (p<0.001). The rates of recurrent CDI in BMAB plus AMAB-treated subjects were not significantly different than in those treated with BMAB alone. The rates of adverse events were similar among the study groups, with diarrhea and nausea being the most common events.

**Reviewer's Commentary:**

It is thought that recurrent CDI results from continued disruption of gut microbiota following treatment of an initial CDI with standard-of-care antibiotics combined with either persistence of resistant \textit{C. difficile} spores or reacquisition of new spores from the environment. Toxins expressed by pathogenic strains of \textit{C. difficile} (toxins A and B) infect epithelial cells of the gut resulting in increases in intestinal permeability and pro-inflammatory responses leading to diarrhea.\textsuperscript{2} Targeting the toxins of \textit{C. difficile} can provide an antibiotic-sparing approach to CDI treatment. Studies have documented that an antibody-mediated immune response to toxin B appears to be strongly protective against \textit{C. difficile} recurrence.\textsuperscript{3} The current study further affirms this in demonstrating that BMAB therapy reduces the risk of a first post-treatment relapse by almost 40% versus that seen with standard therapy. Bezlotoxumab has been recently approved by the Food and Drug Administration. The medication is delivered parenterally and will be expensive. Better assessments of relapse risk for recurrent CDI will be necessary to direct therapy to those patients who will benefit the most.\textsuperscript{4} Additionally, studies have been performed only in adults and any potential use of the treatment in children awaits future investigations in this population. Nevertheless, use of bezlotoxumab may be an effective approach to prevent recurrent CDI.

**References:**

Getting Bugged About the Weather: climate change, the AAP, and you–

Saul Hymes, MD, FAAP
Director of Pediatric Antimicrobial Stewardship, Assistant Professor of Clinical Pediatrics, Pediatric Infectious Diseases, Stony Brook Children’s Hospital

and

Charles Woods, MD, MS, FAAP
Interim Chair, Department of Pediatrics, University of Louisville School of Medicine

While it is hopefully clear to all reading this that climate change is a real problem, it may not be immediately clear what it has to do with pediatrics, or infectious diseases, or even some areas of public health. However, more than just causing longer summers, milder winters, floods, or changing weather patterns, climate change has the potential to cause significant health problems for children across a variety of clinical arenas. In fact, it is already doing so.

To confront this issue head-on, on October 6th-7th of 2016, the AAP Council on Environmental Health (COEH) convened a symposium on the role of climate change on children’s health. Representatives from a variety of AAP Councils and Sections were present, including representatives from the Section on Infectious Diseases (SOID) and the Section on Epidemiology, Public Health, and Evidence (SOEPHE). The aim of the meeting was to establish a baseline of common understanding of the effect of climate change on children’s health and then to create a framework for ideas and actions that the AAP can be involved in and utilize to help tackle this monumental problem, across all sections, all councils, and all levels of AAP leadership.

Many of us are familiar with the damage climate change and its accompanying drastic weather patterns can wreak: the increase in the number of hurricanes, like Katrina or Sandy; the drought in California; and deadly typhoons in the Philippines. But the effect of climate change on children’s health should be no stranger to us either. In 2015, the AAP released a policy statement and technical report, authored by the COEH Executive Committee, on the role of climate change in children’s health. Among the many specific effects of climate change on health, a central point of the document was that children are overall particularly vulnerable to all of the potential health effects of climate change—due to their increased metabolic demands, developing brains and bodies, and increased consumption of food and water for their size. And like all adverse health outcomes across the world, children of low socioeconomic status, who are already even more vulnerable, will be disproportionately affected.

One area in particular where climate change is already having a large effect is the area of infectious diseases. From temperature-related changes in host and vector geographic ranges in the case of vector-borne diseases, to the potential for food and water-borne diseases in disaster settings, it is highly likely that the current wave of novel infections (SARS, MERS), or novel places for old infections (Ebola, Zika) are just the beginning. There are two concrete examples of this occurring as we speak.

The vector-borne bacteria Borrelia burgdorferi, cause of Lyme disease, has spread significantly in recent years. Per graphs available through the CDC (https://www.cdc.gov/lyme/stats/maps.html) one can plainly see the spread of Lyme cases north through upper Minnesota, upper New York State, and Maine. The host range of both the Ixodes tick as well as the white-footed mouse is moving north, correlating with warming temperatures in those areas. On a personal anecdotal level, we have seen our local Lyme disease season on Long Island extend well into November. Even as late as December 31, I have had patients present to the office, picking deer ticks off themselves and their children. Another vector-borne disease, Zika, is gaining a foothold in southern Florida. Because of the historical range of the Aedes aegypti mosquito vector, that is roughly (the southern US) where most epidemiologists believed these tropical vector-borne diseases would stay. But new data (https://www.cdc.gov/zika/vector/range.html) shows the range of this mosquito has expanded north into the Midwest and the mid-Atlantic states, farther than before. Again, this spread correlates with warming temperatures.

The other major potential infectious issue influenced by climate change is the spread of food- or water-borne infections, like Salmonella, or even cholera. After storms like Katrina or Sandy, normal water supplies are compromised. Sewers overflow into sources of drinking water, drinking water may not be accessible, and people may not have access to proper toilets or latrines. All of this makes far more likely the possibility that sewage and human waste in general can contaminate a drinking water supply, or water used to irrigate crops, or even water used to wash produce. The CDC reported an uptick in diarrheal cases after Hurricane Katrina (https://www.cdc.gov/mmwr/Continued on Page 16

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Getting Bugged About the Weather: climate change, the AAP, and you—Continued from Page 15

preview/mmwrhtml/mm5438a6.htm) and similar reports were made after Hurricane Sandy. And larger disasters, which are forecast to only increase as climate change continues (https://www.gfdl.noaa.gov/21st-century-projections-of-intense-hurricanes/), have the potential to displace far more people, with far worse access to clean water, and far more dire health consequences.

There are also a large number of climate change effects that are anticipated to have adverse health effects for children (and across all age ranges) beyond infectious disease outcomes of vector range changes and waterborne infections. Of course, in areas where there are significant annual or seasonal increases in ambient temperatures, increases in heat-related deaths and heat illness is expected. Rising sea levels will lead to encroachment of coastal areas, with increased risk of tidal and storm-related flooding. Similarly, many river valleys and adjacent plains with large population centers will be at greater risk of flooding from tidal, local and upstream weather events. Existing transportation and communication infrastructures will be at risk.

More intense storms and flooding events will cause drownings, injuries, and population displacements, with economic and infection-related consequences. Current food supplies and geographic food production footprints (crops and livestock) may be affected by increases in drought conditions in some areas and more frequent flooding in others. Relocation of crop production may be required in many areas. Algal blooms from flood-related runoffs of fertilizers and other materials into coastal aquatic environments could decimate fisheries and shellfish harvesting in some areas.

Effects on respiratory health, including acute asthma exacerbations and chronic respiratory conditions will result from worsening air quality. Increased air temperature enhances formation of ozone. Wildfires in areas of drought from climate change can raise ozone levels and produce particulates. In areas of increased rainfall and prolongation of growing seasons, increases in pollen counts may be higher and more persistent, with resultant effects on asthma in susceptible individuals.

Children and the elderly will be most vulnerable to all of the consequences of climate change. All of the above infectious and non-infectious effects of climate change can lead to increased mental stresses for individuals and populations of all ages. With worsening mental health and political conflicts, some areas could see new wars develop over real or perceived concerns related to land, housing, food, physical safety, and economic opportunities. More details on these and other potential consequences are available at https://health2016.globalchange.gov/ and https://ecoamerica.org/.

What can you do?

We can all make a difference through policy, advocacy and practice. Samantha Ahdoot, MD, FAAP, lead author of the AAP statement, provides a list of things that pediatricians can do to take action. In addition, there are additional resources and information available on the AAP webpage at: www.aap.org/climatechange. Finally, you can participate in the climatechange@listserv.aap.org. It is open to all AAP members to join and is a way for members to stay informed about what is going on in the world of the AAP, climate change, and kids' health.
Policy Highlights from the Committee on Infectious Diseases (COID)

AAP statements under development or revision
1. Elimination of perinatal hepatitis B – providing the birth dose within 24 hours
2. Infection Prevention and Control in Pediatric Ambulatory Setting
3. Infection Control in Organized Sports
4. Antimicrobial Stewardship in Hospitals
5. Chemical-Biological Terrorism and Its Impact on Children
6. 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. Kawasaki Disease and Endocarditis with Committee on Cardiovascular Disease in the Young (AHA)
3. Diagnosis and Management of Bone and Joint Infections (IDSA/PIDS)
4. Clinical Guidelines for Diagnosis and Antiviral Management of Seasonal and Pandemic Influenza in Adults and Children (IDSA)
5. Infectious Diseases Society of America (IDSA), the American Academy of Neurology Institute (AANI) and the American College of Rheumatology (ACR) clinical practice guideline on Lyme Disease
   a. Subcommittee on Babesiosis
6. Clinical Practice Guidelines Practice Guidelines for Outpatient Parenteral Antimicrobial Therapy (IDSA)
7. Antimicrobial Therapy (IDSA)

From the ACIP Meeting of October, 2016 & February, 2017

The slide sets from the October 19, 2016 meeting and slide sets from the February 22-23, 2017 meeting are available to view. The minutes from these meetings will also be posted on the CDC website. The next ACIP meeting is scheduled for June 21-22, 2017.

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.
In the spring, 2016 Edition of the SOID newsletter, the ID Training Fellows Column discussed the brave new world of rapid diagnostic tests for infectious diseases. An illustrative case shows how the improved sensitivity of the multiplex molecular-based assays\(^1\) can lead to management conundrums that we have not faced previously.

**Case History:** A 17-month old female presents to the clinic one day after visiting the local Urgent Care Center (UCC). She is fully-immunized for age with no known underlying illnesses. At the UCC, the family had reported a one day history of intermittent fever up to 38.4°C. She had 4 episodes of emesis and 12 non-bloody brownish loose-to-watery stools in the prior 48 hours, plus 12 hours of decreased activity and urine output. The child received two IV saline boluses and later did well with a PO challenge. She had two wet diapers during the 8 hour observation, became nonfebrile and more active. She was discharged from the UCC. The UCC clinician advised seeing their PCP the next day.

The toddler had 4 more loose stools after leaving the UCC (mother reports the stools now smell worse than usual). The child is taking PO liquids better and is “more herself”. The mother also reports that the 7-year old brother and the father have had non-bloody diarrhea and some cramping: the brother for 4 days and the father for 2 days. The brother was the first to become ill 3 days ago starting with 4 episodes of emesis on the first day and then 4-6 diarrheal stools for two days. The boy seems “much better”—with no diarrhea in the past 24 hours. The father is still experiencing cramping with 2 emesis episodes and 4 loose stools in the past 12 hours. The mother is starting to have nausea and abdominal cramps.

Your examination reveals an alert, afebrile, well-hydrated but mildly fussy toddler. The only positive findings are somewhat overactive bowel sounds and an irregularly-edged desquamated reddish area in the perianal area without discreet lesions.

**Test Results:** The mother asks about results of the stool test done at the UCC. The UCC clinician told her it would possibly detect the cause of the child’s (and the family’s) gastroenteritis. You find positive results for *Clostridium difficile* and its toxin, norovirus and giardia. Figure 1. The local health department was notified of the giardia results. These are more positive answers than expected. You wonder if this is a gastroenteritis version of the board game Clue\(^6\) because you must now decide which pathogen/s is/are the true cause/s of acute enteritis (norovirus did it in the small bowel!), or is it more like Murder on the Orient Express where there are multiple culprits? More detective work is needed. A review of risk factors for each

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**Figure 1. Panel 1:** *Clostridium difficile* Gram stain (Reproduced with permission from the American Academy of Pediatrics, Red Book Online\(^a\))

**Panel 2:** *Giardia intestinalis* in stool smear (trichrome) (Reproduced with permission from James Brien, MD, FAAP)

**Panel 3:** Norovirus (Reproduced from the CDC Norovirus webpage - [https://www.cdc.gov/norovirus/](https://www.cdc.gov/norovirus/))
of the three possible pathogens (Table 1) in the context of the clinical presentations should hopefully provide more understanding of which one or more “detected” organisms is the true cause.

**Risk Factors.** *C. difficile*: No family member has gastroesophageal reflux, or has recently received antibiotics, antiperistaltics, proton-pump inhibitors or H2-blockers. No one has recently been hospitalized or exposed to anyone with known *C. difficile*. So there is no smoking gun for *C. difficile*. However, recent data indicate that risk factors are not always found in patients with confirmed *C. difficile* disease.

Norovirus: The patient attends a large day care center with >50 attendees divided into pods of 15-18 children each, and further segregated by whether attendees wear diapers or not. Additionally, the family went tent-camping recently. They returned from the “music festival” on the day before the brother became ill. At the festival, there were only portable toilets. The father, mother and toddler shared a juice drink during a hike. The drinks had been cooled off by placing them in a clear running stream. On the last day of the festival, all of the hundreds of attendees shared a communal dinner in the pasture where they had camped. So, there seem to be 5-6 known risk factors for norovirus (large day care, diaper changing station at day care, camping, exposure to ground water, and ingestions of food in a pasture with the food’s origins or cleanliness not being well known).

*Giardia*: Most risks for norovirus are also risks for giardia, i.e. day care, diapering stations, camping, exposure to ground water (streams), and communally shared food in a pasture. Pet presence, particularly cats, at the day care is another risk factors for giardia.

**Management:** Now what to do? Let’s consider each family member separately.

**The 17-month-old:** She had an acute onset and became dehydrated. There was no blood or mucous in the stools, although mother reports that the toddler’s stools are now foul-smelling. Toddlers < 2 years old are well known to have high rates of *C. difficile* colonization (up to 35%). Given the toddler’s improvement with no intervention that should eradicate *C. difficile*, it seems reasonable to conclude that this episode was not caused by *C. difficile*. Further, it seems unlikely that *C. difficile* would cause a rapidly sequential family outbreak. So, the *C. difficile* in this case is likely a colonizing organism not responsible for the child’s disease.

She was acutely symptomatic with both vomiting and non-bloody diarrhea. This presentation is fairly classic for norovirus and she has multiple risk factors for norovirus. Coupled with the timing in relation to the family camping experience, norovirus seems a likely culprit. The acuity of presentation seems more severe than one might expect if giardia was the solo true cause. But, she has so many risk factors for giardia (shared with norovirus) that a dual infection/infestation may be the answer, particularly if the foul smelling loose stools continue.

**The 7-year-old:** He was the index case but is nearly well now with no diarrhea in 24 hours. It is unlikely he has active *C. difficile* disease. But he likely had acute norovirus gastroenteritis. While he still could have a giardia as a component, no intervention and a period of further observation seem in order for him. If he has more loose stools, bloating or abdominal pain more than a few days into the future, testing for giardia antigen (less expensive than the multiplex PCR) would resolve whether giardia was also involved.

**Father:** The father also is improving. He became ill the day after the brother. The same approach as for the brother seems reasonable for Dad.

**Mother:** She is just beginning her symptoms. If it is norovirus, no intervention is needed. If giardia is involved, she may need treatment. So, you counsel her to contact her PCP if symptoms persist longer than the 2-4 days, usually associated with norovirus, or if she develops acute symptoms of dehydration or severe persisting emesis.

**Three days later:** The health department notified the family that a norovirus outbreak occurred among festival attendees (nearly 65% attack rate). This was discovered during follow-up of the positive giardia results in the toddler. A lesser outbreak of giardia (20% attack rate) also occurred among those partaking of the stream-cooled juice drinks. However, stool from father, mother and the 7-year-old was tested by the health department and only the toddler has giardia in this family. The toddler is still having 3-4 loose bad-smelling stools and appears to have extra flatulence with some abdominal discomfort.

*Continued on Page 20*
Drug treatment. So now the question is, do you treat the 17-month old’s giardia? The answer is, yes. (If all the symptoms had abated, one could make the case for continued observation.) Tinidazole would be the drug I would use. It is a one-dose, relatively convenient treatment. The dose is 50 mg/kg up to a maximum of 2 grams. It can be and probably should be taken with a food chaser to help blunt the less than pleasant taste. A suspension can be made by a certified pharmacy by crushing tablets (250 mg each) and suspending the powder in artificial cherry syrup to make a final concentration of 67 mg/mL. This suspension must be shaken well before a dose, but is stable without refrigeration for 1 week. Retail costs without insurance average about $80 with co-pays estimated at around $30. Eradication rates are between 85 and 90% with a single dose.\textsuperscript{22, 23}

Ok to go back to Day care? Can she go back to day care when she no longer has diarrhea? The answer is yes. Norovirus’ exclusion is for duration of illness. Giardia carriage rates of up to 50% have been reported in US day care centers with the highest rates in the southern region of the United States. However, it is beneficial to review day care procedures for cleaning up stool leakages and emesis. Using paper towels without a disinfectant or soap may increase risk of transmission. Clorox-based disinfection, when possible, of toys, mats, diapering areas, etc. can also reduce transmission risk. Some experts also recommend soap and water hand hygiene rather than alcohol based de-germers after cleaning up vomit to stool because alcohol-based de-germers may not be sufficient.

Conclusion: If your laboratory uses a multiple gastroenteritis panel, you may see more and more multiple positive results. Deciding on management and interventions can be challenging. Hopefully, good detective work, ongoing symptom observation, and appropriate re-testing for individual pathogens can lead you to the true culprits in your patients.

<table>
<thead>
<tr>
<th>Table 1. Risk Factors for Detected Pathogens</th>
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<tbody>
<tr>
<td><strong>C. difficile</strong></td>
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<tr>
<td>Recent antibiotics</td>
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<tr>
<td>Antiperistaltics</td>
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<tr>
<td>Proton pump inhibitors</td>
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<tr>
<td>H-2 blockers</td>
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<tr>
<td>Recent hospitalization</td>
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<tr>
<td>Frequent contact with healthcare facilities</td>
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<tr>
<td>Exposure to known C. difficile infected person</td>
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<td>Carriage at young age (mostly &lt; 2 years)</td>
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</tbody>
</table>

References:
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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

I. AAP

   1. These are broad spectrum agents that should be used selectively in specific clinical situations.
      a. Infection caused by multidrug-resistant pathogens for which there are no safe and effective alternatives.
      b. There are no non-fluoroquinolone oral therapies available and oral treatment is preferred.
   2. Reviews safety studies in children/adults and reviews resistance data.
   3. Adverse reactions are uncommon, however; because of the risk of peripheral neuropathy, CNS effects, cardiac, dermatologic and hypersensitivity in adults, in July 2016, the FDA issued box warnings restricting use to only when no other alternative was available.


   1. The above link includes the specific changes have been made to the 2017 schedule.

II. MMWR
A. Recommendations for Use of Meningococcal Conjugate Vaccines in HIV-Infected Persons- Advisory Committee on Immunization Practices, 2016. MMWR November 4, 2016/65(43);1189-1191.
   1. ACIP added HIV to the list of medical conditions that have an increased risk for meningococcal disease.
   2. Other prior conditions include: complement deficiency, persons receiving eculizumab for the treatment of atypical hemolytic uremic syndrome, functional and anatomic asplenia.

B. Use of a 2-Dose Schedule for Human Papillomavirus Vaccination- Updated Recommendations of the Advisory Committee on Immunization Practices. MMWR December 16, 2016/65(49);1405-1408.

C. Guidance for Assessment of Poliovirus Vaccination Status and Vaccination of Children Who Have Received Poliovirus Vaccine Outside the United States. MMWR January 13, 2017/66(1);23-25.


E. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older- United States, 2017. MMWR February 10, 2017/66(5);136-138.

III. IDSA


Continued on Page 24
New Policy/Guidelines Continued from Page 23

1. Recommendations for management of children and adults.
2. Due to public health implications, managing a patient with a public health case manager is recommended to help maintain treatment adherence.

   1. Use of IGRA and TST for latent tuberculosis infection (LTBI) and acid-fast bacilli smear microscopy, liquid and solid mycobacterial cultures and NAAT to help determine TB disease are discussed.

   2. Added are additional recommendations for diagnosis and managing early infections.
   3. Additional management for coccidioidomycosis meningitis.
   4. Surgical management recommendations are discussed.
   5. Specific at-risk groups discussed (eg. HIV, solid organ transplants and pregnant women and their neonates).
   6. Sections on lab-accident management.

E. **Diagnosis and Treatment of Leishmaniasis: Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene** (ASTMH). *Clin Inf Dis* 2016;63: 1539-1557.
   1. Approaches to diagnosis/management of cutaneous (CL), mucosal (ML) and visceral leishmaniasis (VL).
   2. CL is most common in North America and skin lesions are painless and chronic.
   3. VL reflects dissemination and can be life-threatening.

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

A. Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents.
   1. Updated July 2016.
   2. New approval drug Tenofovir alafenamide and emtricitabine (TAF/FTO) for anti-retroviral naive patients.

B. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents.
   1. Updates on treatment of coccidioidomycosis and cryptococcosis.

   1. Updated October 2016.
   2. Initiation of ART as early as possible in pregnancy since ART during pregnancy does not increase risk of birth defects.
   3. Changes in initial combo regimens for ARV naive-pregnant women.
   4. Updates newborn delivery recommendations and infant ARV prophylaxis.
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