



# INFECTIOUS DISEASES

Volume 26, Issue 2

NEWSLETTER

Fall/Winter 2023

## Chair's Letter



Welcome to the Fall SOID newsletter. I would like to call your attention to the number of great articles in the newsletter, including updates on RSV prevention, clinical pearls and our fellow's corner. I know it is extra work for all these extremely busy people so I am appreciative of the time they have taken to bring us updates on these very important topics. As I write this, I am looking at the calendar and realizing we soon will be in "fellowship season". While not QUITE as daunting as the issues we face with weather changes, pediatric infectious diseases is facing a significant climate change. For the last few years, many Pediatric Infectious Diseases fellowships went unfilled. For the 2022 interview season (for fellowships starting July 2023), of the 81 positions available, only 40 were filled. I am hoping that we see a reversal in the trend this year. However, to make that happen, we need more than hope.

We need to be proactive and promote our specialty. The earlier we expose our trainees to infectious diseases as a sub-specialty, the better our chances of having them choose ID as a career. At our institution, we recently have introduced "meet the physicians" for medical students. In an informal setting, we talk about ID as a career and start dialogues with the students. While the program still is young, we have seen an increase in the number of students attending the sessions which may translate into more students choosing pediatrics as a residency and subsequently infectious diseases for fellowship training.

With the high level of debt many young physicians have accumulated, I understand there could be concern about salary associated with our specialty. Efforts are underway to improve the salary structure in Pediatric Infectious Diseases and Pediatrics as a whole. In a growing number of programs, the salaries of pediatric sub-specialties are being benchmarked to the salary of the same sub-specialty in internal medicine. However, as our HR Department likes to say; "You need to look at the whole package and salary is one factor (albeit an important one)." Along that line, I am hearing many young physicians stress the importance of "work-life balance"

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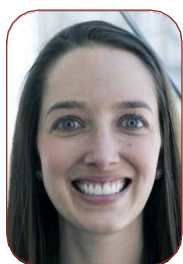
## Chair's Letter *Continued from Page 1*

and job satisfaction. We need to have physician trainees see the number of potential careers within infectious diseases which allows multiple avenues to a fulfilling career. In addition to being a successful clinician, opportunities exist in Infection Prevention and Control, Antibiotic Stewardship, Travel Medicine to name a few. Beyond clinical medicine, there also are exciting careers in basic science and clinical research. As we have seen from the recent pandemic, there is no shortage of information that still needs to be generated regarding the prevention and treatment of infectious diseases.

So, I ask each of you to spread the excitement for infectious diseases and to encourage our physicians-in-training to consider our specialty as a career. I also encourage suggestions from our community as to how to raise awareness and interest in infectious diseases as a career. I look forward to hearing from you!

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## Welcome to new SOID Executive Committee Training Fellow Liaison



**Melissa Day, MD**, is a second-year pediatric infectious diseases fellow at Cincinnati Children's Hospital Medical Center. She obtained her undergraduate degree from Duke University and her medical degree from Vanderbilt University School of Medicine. She completed her pediatric residency training at Cincinnati Children's Hospital Medical Center. Her research interests include understanding health disparities across all aspects of infectious diseases, with a particular interest in antimicrobial stewardship. During her fellowship, Melissa is pursuing a Master of Science in Clinical and Translational Research at the University of Cincinnati. She was recently awarded the Pediatric Infectious Diseases Society (PIDS) Stanley and Susan Plotkin and Sanofi Pasteur Fellowship Award to pursue further investigation into caregiver adversity, socioeconomic deprivation, and infection-related outcomes in vulnerable pediatric populations. These research experiences will serve her well as she plans to pursue a career

as a physician scientist to continue to explore the epidemiology and associations of health disparities in infectious diseases to improve pediatric health outcomes. When Melissa has free time, she enjoys hiking and camping in local state/national parks, trying new restaurants, and traveling.

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## Welcome to new SOID Education Subcommittee Training Fellow Liaison



**Shreya Doshi** is a second-year pediatric infectious diseases fellow at the Children's National Hospital, DC. Originally from Mumbai where she went to medical school, Shreya has spent the last 5 years in the DC area. She is interested in antimicrobial/laboratory stewardship but also has a passion for learning more about sustainability/ climate change and its impact on infectious diseases. She recently received the Pediatric Infectious Diseases Society (PIDS) Antimicrobial Stewardship Fellowship Award at ID week, in October 2023. She is also the co-founder of "Sustainabil-ID", a committee for infectious diseases physicians, pharmacists and trainees that meets once a month to talk about how we can integrate environmental sustainability into various infectious diseases practices. Her overarching career goal is to blend these interests into global health. She is currently studying global health and epidemiology at GWU. When she isn't "geeking" out about an infectious diseases fun fact at the hospital, you

can find her dancing, singing, playing the acoustic guitar within the confines of her home or exploring cute cafes and restaurants in Washington DC with friends and family.

## Protecting Children from COVID-19: Perspective from a Frontline Pediatrician

*Michelle D. Fiscus, MD FAAP, Chief Medical Officer, Association of Immunization Managers*

We have all seen how COVID-19 vaccination coverage rates for children have languished, especially for children under age 5 years. With the movement of COVID-19 vaccines to the commercial market and the arrival of new XB.1.5 Omicron subvariant vaccines for the fall/winter respiratory virus season, now is the time to redouble our efforts and get children vaccinated.

Since the start of the global pandemic in 2020, [more than 2,300 children have died](#) from COVID-19-related illnesses. That number is vastly higher than the number of deaths from other diseases we routinely vaccinate against, such as measles, polio, and pertussis, and yet, we are largely failing to encourage parents to vaccinate their children against a disease that nearly 100 percent of them will contract in infancy. And death, of course, is not the only concern. Viruses have a track record of causing terrible disease much later in life. [Subacute sclerosing panencephalitis](#) (SSPE), for example, usually occurs in children infected with measles prior to age 2 years but takes approximately 6-8 years to develop. If not treated, one in four infants infected with [hepatitis B](#) at birth will die prematurely from cirrhosis or liver cancer. And, post-herpetic neuralgia and other complications from herpes zoster typically do not appear until decades after a primary [varicella](#) zoster infection. We are in year four of SARS-CoV-2. Why are we not protecting babies when we have safe and effective vaccines that will not only help prevent hospitalization and death, but also may prevent significant sequelae? The answers are complex.

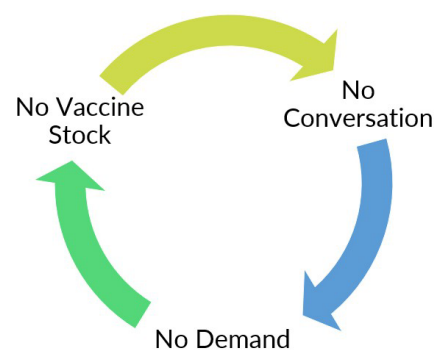
Pediatricians are fatigued. Tired of being understaffed and underpaid. Tired of engaging in conversations with parents who have made up their minds that, despite our evidence-based recommendations, they are not going to give their children “that COVID-19 shot”. We are tired of fighting. But here is the thing: every day in this country approximately 10,000 babies become 6-month-olds who are newly eligible to get vaccinated. Many of those parents may have never had a conversation with their child’s pediatrician about getting vaccinated against COVID-19. Without those conversations, the message they receive from us is that this vaccine is not important. I hear from pediatricians every day that they do not stock the vaccines because “there’s no demand”. It’s a circular argument—we don’t have the conversations, there’s no demand, we don’t stock the vaccines, we don’t have the conversations.

It’s time to treat COVID-19 vaccines as we have treated every other vaccine recommended by the CDC and the Advisory Committee on Immunization Practices (ACIP)—put it into the routine schedule and make a strong recommendation that parents vaccinate their children.

We learned hard lessons from human papillomavirus vaccine (HPV)—destigmatize the disease, use presumptive language, and sandwich the HPV vaccine between Tdap and meningococcal vaccines when making the recommendation to parents. We should be doing the same for COVID-19 vaccines. Let’s start the conversation at the 4-month well-child visit: “Next time I see you, your baby will get their last round of baby shots and we’ll start the COVID-19 vaccine series.” Give them printed information and, if the mother was vaccinated against COVID-19 during pregnancy, talk about how the protection she gave her baby while she was pregnant is going away and how we need to continue that protection with a vaccine. Preventive or ‘well-child’ visits need to allow time for questions and explore concerns the parents may have around the topic of vaccinations. When the baby comes in for the 6-month well-child visit they should hear, “Today your baby is due for diphtheria/tetanus/pertussis, *Haemophilus influenzae type b* (Hib), pneumococcal, COVID-19, polio, rotavirus (depending on the timing of the vaccine you use), and flu (depending on season) vaccines.” As providers, we should consider that often times, parents’ questions or even direct ‘pushback’, come from a place of fear about making the wrong decision on behalf of their child’s health. We need to reassure them that anxiety is normal and that you both want the same thing—for their baby to be healthy. If they still decline the vaccine, give them some resources and tell them how important you think this is and that you’ll talk about it again next time. Treat COVID-19 as you would any other recommended childhood vaccine.

With the movement to the commercial market, COVID-19 vaccines are easier than ever to have in the pediatric office. Some manufacturers have single dose vials, eliminating the liability from wastage. Minimum orders are as low as 10 doses for some age groups. Ultra-cold

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## Protecting Children from COVID-19

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freezers are no longer needed. The number of different formulations and the number of injections have been significantly reduced. It is time to normalize these vaccines and get babies protected. Pediatricians are the leading experts in talking with families about vaccines. Let's not look back in a few years and say we wish we'd tried harder with this one.

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## A Review and Update of Key Vaccine-Preventable Childhood Infections

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## Recognizing Vaccine-Preventable Childhood Infections

Immunization rates plummeted during the first 1–2 years of the COVID-19 pandemic. In 2022, over 20 million children around the world remained undervaccinated, with 14 million children vaccine-naïve.<sup>1</sup> By 2023, global vaccine rates have begun to improve. The WHO reported an increase in single-dose MMR vaccination rates from 81% to 83% in children by age 2 years, but this remains below the 86% level from 2019. Receipt of the third dose of DTaP or DTP, a marker of childhood immunization administration, increased from 81% in 2021 to 84% in 2022.<sup>2</sup>

Nationally, immunization rates for the United States (US) remain below pre-pandemic levels and declined nearly another 1% in the 2021–2022 school year.<sup>3</sup> Two-dose MMR immunization uptake is 93% in the US, which remains below the 95% level required for community (herd) protection.<sup>3</sup> With fewer children receiving the recommended childhood vaccinations, the medical community is more likely to encounter cases of measles, mumps, rubella, varicella, and pertussis. Children first come to medical attention at their primary provider's office, an urgent care center, or a hospital emergency department. Physicians who likely have never seen these infectious conditions will need to be able to identify and provide recommendations. This article aims to provide preliminary guidance for managing vaccine-preventable infections in the pediatric population. Data are summarized in the Table. For additional in-depth information and recommendations for special situations, see the AAP's [Red Book: 2021–2024 Report of the Committee on Infectious Diseases](#) or the CDC's [Immunization website](#).

### MEASLES VIRUS

Measles classically presents with high fever, copious exudative conjunctivitis, rhinitis, and severe cough that precedes the onset of a maculopapular rash on the face and neck. As the rash becomes more confluent, it also extends cephalocaudally. The rash persists for approximately one week, and mild desquamation can occur with resolution.<sup>4</sup> Enlarged cervical lymph nodes also can accompany these symptoms. Koplik spots, i.e., pinpoint white papules on the erythematous buccal mucosa opposite the pre-molars, are the hallmark enanthem that can accompany early symptoms. The most common acute complications of measles are viral interstitial pneumonia and acute encephalitis as well as secondary bacterial pneumonia. Many experts recommend treatment with Vitamin A supplementation in US children with measles for a 2-day period, which has been shown to decrease mortality in children in resource-limited countries.<sup>5</sup>

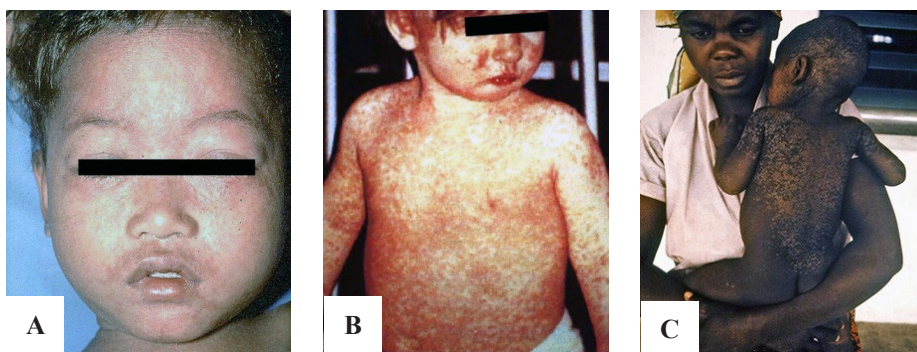
There is currently no measles virus monovalent vaccine. The effectiveness of a single dose of the measles-mumps-rubella vaccine (MMR) at 12–15 months of age against measles is 93–95% and with the second dose approximates 97%.<sup>4,6</sup> In addition to the universal recommendations, international travelers also should be evaluated for the need for MMR. All infants ages 6 through 11 months of age who are traveling internationally should receive a dose of MMR at least 2 weeks before departure. Any dose administered before 12 months of age does not count toward their 2-dose series, which should begin at 12–15 months of age, and at least 28 days after their earlier

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## Recognizing Vaccine-Preventable Childhood Infections *Continued from Page 4*

dose. Children older than 12 months of age and adults who have received a single dose of MMR should receive their second dose before travel, provided that the interval between doses is at least 28 days.<sup>5</sup> Measles is still endemic in most countries that do not have contiguous borders to the US. While it is not an exhaustive list, recent measles cases have been imported to the US from the Philippines, Ukraine, Israel, Thailand, Vietnam, England, France, Germany, and India.<sup>4</sup>



**Figure 1** A) Maculopapular rash on the face in a child with measles B) Confluent maculopapular rash on fair skin C) Skin desquamation can occur in the recovery stage of measles.<sup>4</sup>

### MUMPS VIRUS

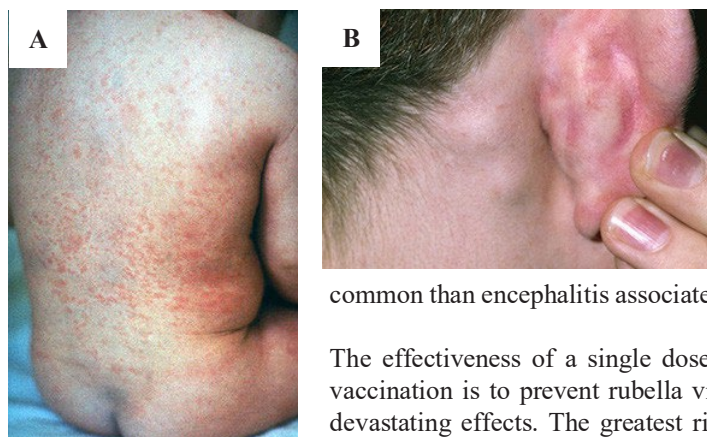


Prodromal symptoms of mumps are nonspecific and include low-grade fever, fatigue, and possible URI symptoms. The classic presentation of mumps is parotitis, i.e., tender swelling that obliterates the angle of the jaw, which can be unilateral or bilateral. Edema of salivary glands and earache can occur as well. Parotitis persists for an average of 5 days but may take longer than 1 week to resolve. Potential complications are more common among post-pubertal adolescents and adults. These include mastitis, orchitis, oophoritis, pancreatitis, meningitis, encephalitis, and hearing loss.<sup>7</sup> Treatment is supportive.

While the effectiveness of a single dose of MMR against mumps is 78%, two doses increase effectiveness to 88%.<sup>5</sup> The resurgence of mumps in the US in the last decade has occurred primarily in college-aged young adults and persons who previously received 2 doses of MMR, suggesting a waning of vaccine-induced immunity.<sup>8</sup>

**Figure 2** Parotitis in a young child with mumps<sup>3</sup>

### RUBELLA VIRUS



Infection with rubella virus is subclinical in nearly half of infected individuals. When symptomatic, low-grade fever, fatigue, and adenopathy often precede the appearance of a pruritic maculopapular rash. Compared with the rash of measles, the rash of rubella classically is less erythematous and does not become confluent. The cephalocaudal progression and distribution of enlarged lymph nodes are the same as for measles. Complications of rubella include thrombocytopenia purpura and organ hemorrhage (cerebral, renal, or GI). While encephalitis can occur, it is less common than encephalitis associated with measles virus infection.<sup>5</sup>

The effectiveness of a single dose of MMR is 97% against rubella.<sup>5,8</sup> The main objective of rubella vaccination is to prevent rubella virus infection in pregnant persons as infection of the fetus can have devastating effects. The greatest risk to the fetus is the acquisition of rubella in the first 12 weeks of pregnancy.

**Figure 3.**

A) The maculopapular rash of rubella is milder and less confluent than measles.<sup>8</sup>

B) Enlargement of posterior auricular lymph nodes can occur in both rubella and measles.<sup>9</sup>

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## Recognizing Vaccine-Preventable Childhood Infections *Continued from Page 5*

### VARICELLA ZOSTER VIRUS

Primary infection with varicella zoster virus (VZV) causes varicella (chickenpox); reactivation causes herpes zoster (shingles). Varicella infection can manifest with a fever up to 102°F for a few days accompanied by other systemic symptoms. The rash then appears on the face or trunk, rapidly becomes generalized and is extremely pruritic. Lesions often begin as macules, transition to papules and vesicles (“dew drop on a rose petal”), and eventually become dry and crusted. The typical 250–500 lesions seen in unvaccinated persons are in various stages of evolution. Children are considered infectious until all lesions have crusted.<sup>5</sup>

Breakthrough varicella is defined as a wild-type VZV infection in a vaccinated person 6 weeks or more after immunization. The infection is milder compared with wild-type VZV infection in unvaccinated individuals. Fever is absent or low grade. Only 50 or fewer lesions appear successively and are predominantly maculopapular without evolution to vesicles or crusts. Breakthrough VZV infection still is contagious.<sup>10</sup> Occasionally, vaccine strain VZV can lead to several skin lesions in the weeks following vaccination with transmission to unvaccinated contact occurring rarely.

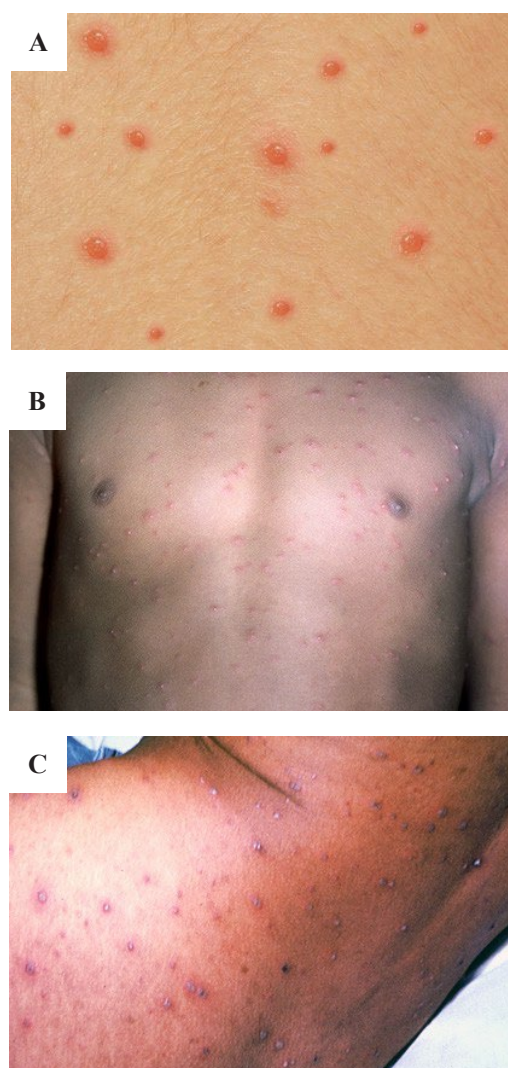
The most common complication of varicella in children is secondary bacterial infection of the skin and soft tissues. Interstitial viral pneumonia can occur but is more common in adults. Other complications include secondary bacterial pneumonia, cerebellar ataxia, encephalitis, secondary bacterial toxic shock syndrome, and serious skin and bone infections.<sup>5,10</sup> Varicella is especially associated with secondary infection from *Streptococcus pyogenes* and *Staphylococcus aureus*.<sup>5</sup> Varicella in immunocompromised children can lead to life-threatening visceral dissemination, and severe interstitial pneumonia.

Nonspecific therapies for preventing spread of varicella include trimming fingernails, frequent bathing, application of lotion to reduce pruritis, and acetaminophen for uncomfortable fevers.<sup>5</sup> Salicylates must be avoided, and ibuprofen also should be avoided. The effectiveness of antiviral therapy in otherwise healthy individuals is limited to commencement during the first few days after rash onset. Oral valacyclovir usually is prescribed for unvaccinated people over 12 years of age in whom the course of chickenpox typically is more severe. Acyclovir intravenously is given to immunocompromised people of any age and even when recognized  $\geq 3$  days after rash onset.<sup>6</sup> Antiviral therapy should be considered for patients at increased risk of moderate to severe varicella or its complications. In addition to otherwise healthy adolescents, these include persons with chronic pulmonary or cutaneous disorders

and those receiving long-term salicylates, corticosteroids or other immune-modulating therapy.<sup>5,10</sup>

Herpes zoster represents the reactivation of VZV that remained latent in the dorsal root ganglia after primary VZV infection. Prodromal symptoms often are nonspecific. The affected dermatome(s) may be pruritic, exquisitely painful, or accompanied by paresthesia. Characteristically, herpes zoster is expressed on 1–2 adjacent dermatomes. Vesicles erupt and cluster over 3–5 days before crusting.<sup>5</sup> Lesions can lead to scarring or changes in pigmentation. Resolution of pain can take weeks. On occasion, vaccine-strain VZV can be the cause of herpes zoster in immunocompetent and immunocompromised people, occurring less frequently following vaccination than following natural infection.

One of several possible interventions should be recommended for exposed and under- or unvaccinated people who are healthy. The first consideration is varicella vaccination as soon after exposure as possible (up to 5 days post exposure). Vaccination in this manner protects against clinical varicella from the current exposure as well as potential exposures in the future. If vaccination is not possible, pre-emptive oral acyclovir or valacyclovir therapy is begun on day 7 after exposure. Post-exposure prophylaxis using Varicella Zoster



**Figure 4** Vesicles of primary varicella on fair skin (A) and (B) darker skin (C) Crusted lesions<sup>9</sup>



## Recognizing Vaccine-Preventable Childhood Infections *Continued from Page 6*

Immune Globulin ([www.varizig.com](http://www.varizig.com)) is indicated when the exposed person likely is susceptible to VZV, the exposure likely would transmit infection, and infection would be suspected to be severe. Such persons include immunocompromised, pregnant persons, and certain neonates.<sup>5</sup>

Since its implementation in 1995, the vaccination program for varicella has been highly successful. The effectiveness of the two-dose schedule of the VZV vaccine against varicella is 90–92%. A single dose provides 82% protection against infection and 98–100% against severe infection. The second dose increases the degree and duration of protection.<sup>5,6</sup> Universal vaccine has provided community protection by reducing VZV circulation, thus reducing the risk of acquisition for persons unable to receive the live virus vaccine due to age or health status.<sup>10</sup>

### ***BORDETELLA PERTUSSIS***

Classically in the unvaccinated child, the severity and character of symptoms from infection caused by *Bordetella pertussis* depend on the patient's age and stage of seeking medical attention. Pertussis has three clinical stages: catarrhal, paroxysmal, and convalescent. The catarrhal phase is relatively mild compared with viral upper respiratory infections, with cold-like symptoms and a possible low-grade fever. A cough usually develops within the first 1–2 weeks after the onset of symptoms. This is followed by the paroxysmal stage, characterized by coughing “fits” with high-pitched inspiratory “whoops.” Post-tussive emesis and cyanosis can occur in this phase. The paroxysmal stage can last 1–6 weeks, or occasionally months, before transitioning to the convalescent stage. This last stage follows a slow pace of diminution in frequency and severity of coughing spells. Children can have a recurrence of the characteristic coughing spells with subsequent URIs in the months after symptom resolution, which is not due to reactivation of *B. pertussis*.<sup>5,11</sup>

Pertussis in the young infant has foreshortening of the first stage. After a few days of URI symptoms, there is a sudden onset of gagging, gasping, and cyanosis. Risk of apnea or inability to self-rescue occurs during the catarrhal and early paroxysmal stage given the young infant's limited ability to expel respiratory secretions. The mortality of pertussis is almost entirely limited to infection prior to 3 months of age. Very young infants and prematurely born infants are prone to development of pulmonary hypertension and ensuing cardiopulmonary failure. Apnea is an early cause of death. Secondary bacteria pneumonia, seizures, and encephalopathy associated with hypoxemia also can complicate the course in infants.<sup>6</sup>

Adolescents and adults with pertussis have no distinct stages of illness and cases are greatly unrecognized. Pertussis should be suspected in persons with a pure or predominant coughing illness that is escalating at 1–2 weeks from illness onset, regardless of history of immunization. The clue to diagnosis is the severity and duration of the cough. Coughing paroxysms frequently are heralded by the feeling of impending strangulation and can end with vomiting.<sup>5</sup>

Diagnosis of pertussis in the catarrhal and early paroxysmal phase usually is made clinically and confirmed by nasopharyngeal PCR testing for *B. pertussis*. After the first few weeks of cough, *B. pertussis* PCR result often is negative. In previously immunized individuals, the PCR positivity rate is lower and the duration of positivity is shorter. Serologic testing can be performed up to 3 months from cough onset. People with symptomatic infection will have elevated serum IgG antibody against *B. pertussis* toxin that is clearly higher than expected following distant vaccination with DTaP or Tdap. If a complete blood count is done, more severe infections may have lymphocytosis with absolute lymphocyte counts of more than 20,000 cells/ $\mu$ L.<sup>11</sup>

Antibiotic therapy is recommended for all people with pertussis who are within 21 days of the onset of illness. Azithromycin is the drug of choice and should be used instead of erythromycin for infants to lessen the risk of drug-associated pyloric stenosis. Therapy renders the patient noncontagious after completion of 5 days and may alter the clinical course of illness if given within 5 days of symptom onset. Azithromycin is recommended for all close contacts regardless of immunization history.<sup>5</sup> Underimmunized children who are under the age of 7 years should be given any required doses of the DTaP series. Underimmunized children 7 years of age and older should be given at least one dose of Tdap. Previously DTaP-immunized older children can be given an “early” dose of Tdap. If administered before 10 years of age, they should still receive the universally recommended Tdap dose at 11–12 years of age. Adolescent and adult contacts who received Tdap at 11–12 years are not recommended to receive a second dose.<sup>5,11</sup>

Pertussis remains common worldwide, including in the US. The acellular vaccine provides only 80–85% effectiveness against prolonged coughing illness at the completion of dose 5; protection following DTaP and Tdap wanes rapidly.<sup>11</sup> The reactogenicity of whole cell

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## Recognizing Vaccine-Preventable Childhood Infections *Continued from Page 7*

pertussis vaccines implemented in 1948 prompted the development and transition to more purified acellular vaccine preparations, which are better tolerated but drive a predominantly Th2 rather than a Th1 immunologic response. The decline in immunizations overall, high infectivity of *B. pertussis*, and waning of DTaP and Tdap-associated immunity are likely contributing to the increasing number of cases of pertussis in the US.

**Table 1. Summary of Facts about Vaccine-Preventable Infections, their Management, and Prevention**

Vaccine-preventable infection	Clinical Presentation	Diagnostic Testing	Management	Vaccine and % Effectiveness	Annual US cases/year
<b>Measles virus</b>  (rubeola, measles)	High fever, conjunctivitis, coryza, cough, +/- Koplik spots. Cephalocaudal progression of maculopapular rash, coalescing and persisting for 3+ days	Measles IgM or PCR on serum/plasma specimen. Additional measles PCR can be performed on nasal, NP, or throat and urine specimens to increase the diagnostic yield	PO Vitamin A:  - 50,000 IU per dose q24h x 2 if < 6 months  - 100,000 IU per dose q24h x 2 if 6-11 months  - 200,000 IU per dose q24h x 2 if ≥ 12 months of age <sup>6</sup>	1) Two doses of MMR are 98% protective  2) Single dose of MMR is 93–95% protective. <sup>4,6</sup>	Cases vary by year: 1274 in 2019, 13 in 2020, 49 in 2021, 121 in 2022 <sup>4</sup>
<b>Mumps virus</b>  (mumps)	Low-grade fever, non-specific prodrome, URI symptoms, parotitis	Mumps PCR performed on buccal swab or urine specimen. Serum IgM antibody testing for mumps is recommended 3-10 days after onset of parotitis. Positive mumps IgM by itself does not confirm the diagnosis <sup>5</sup>	Supportive	1) Two doses of MMR are 88% protective  2) Single dose of MMR is 78% protective	Large outbreaks in close-contact settings in 2006, 2009-2010, and 2015-2019 <sup>9</sup>
<b>Rubella virus</b>  (German measles)	Low-grade fever, conjunctivitis, rhinitis, cough, lymphadenopathy. Maculopapular rash that extends cephalocaudally, not coalescing	For postnatal cases: IgM antibody performed on serum, or significant increase in rubella IgG antibody in two serum specimens; PCR on nasal/throat specimen	Supportive	1) Two doses of MMR vaccine probably lead to lifelong protection  2) Single dose of MMR is 97% protective <sup>5,8</sup>	Endemic rubella and congenital rubella syndrome have been eliminated in the US. Imported cases have occurred sporadically since 2012 <sup>5,9</sup>
<b>Primary infection varicella zoster virus</b> (chickenpox)	Fever 2-3 days, generalized pruritic rash: macules → papules → vesicles → crusts	VZV PCR performed on specimens from unroofed vesicle or crust	PO valacyclovir or acyclovir for otherwise healthy persons who are high risk for severe disease (e.g., ≥12 years of age; chronic cutaneous or pulmonary disease; corticosteroid or salicylate use) <sup>5</sup>  IV acyclovir for immunocompromised hosts, including those receiving corticosteroids for >14 days		8200–8800 cases of chickenpox annually between 2017–2019 <sup>11</sup>
<b>Reactivation varicella zoster virus</b> (shingles)	Unilateral vesicles clustered within 1-3 contiguous sensory dermatomes +/- pain, pruritis	Clinical diagnosis. Confirmatory testing with PCR performed on specimen of lesion (as above) if lack of immunity or high risk of severe disease	Consider antiviral therapy for children with zoster and continuing development of new lesions	Two-dose series of Zoster vaccine (Shingrix) is indicated universally for adults ≥50 years of age	Rare; < 0.35 per 1,000 persons <3 years of age in 2016 (with 90–92% population coverage with 2-dose VZV vaccine). Reactivation of vaccine VZV is less frequent than following primary varicella. <sup>12</sup>

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## Recognizing Vaccine-Preventable Childhood Infections *Continued from Page 8*

**Table 1. Summary of Facts about Vaccine-Preventable Infections, their Management, and Prevention (Continued)**

<b><i>Bordetella pertussis</i> (whooping cough)</b>	Paroxysmal stage: coughing bursts with post-tussive whoop +/- cyanosis, vomiting	<i>B. pertussis</i> PCR performed on nasopharyngeal specimen. PT IgG antibody in serum is used to confirm diagnosis in later stages	Azithromycin x 5 days <sup>6</sup>	A 5-dose series of DTaP before 7 years of age or single dose of Tdap in older children is 80-85% protective against coughing illness of $\geq 3$ weeks duration. Protection wanes rapidly <sup>11</sup>	Cases vary by year and cycles: 18,617 in 2019, 6124 in 2020, and 2116 in 2021 <sup>11</sup>
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## Recent Increase in Invasive GAS Infections

Melissa Day, MD, FAAP; Shreya Doshi, MD, FAAP; Jonathan Mannheim, MD, FAAP

### Background:

On December 15, 2022, the World Health Organization (WHO) published a news item describing large increases in the number of invasive group A *Streptococcus* infections (iGAS) throughout Europe, including an increase in iGAS deaths.<sup>1</sup> Children under the age of 10 years were the most affected. One week later, the Centers for Disease Control & Prevention (CDC) Health Alert Network published a health advisory reflecting the same concerns in the United States (US).<sup>2</sup> In the months since, buoyed by an abundance of research into the increase in iGAS infections, numerous local and national health departments around the world continue to issue health advisories on the increase in iGAS. The core of this research is underlined by the same question: Why is this happening?

The dreaded “strep throat” has been a part of pediatrics as long as there have been pediatricians. Hippocrates wrote about erysipelas in the 4th century BC, and Galen noted its inflammatory and infectious properties in the second century AD.<sup>3</sup> *Streptococcus pyogenes* is the principal bacterial species bearing the Lancefield group A antigen, and is therefore often termed group A *Streptococcus* (GAS).<sup>4</sup> It is a frequent cause of acute pharyngitis in school-aged children, and it is the most common bacterial cause for this infection.<sup>5</sup> Additionally, GAS infections have been associated with subsequent complications including acute rheumatic fever, acute glomerulonephritis, suppurative cervical adenitis, and retropharyngeal abscess.<sup>6</sup> GAS infections can also be the etiology for such skin infections, as impetigo, erysipelas, and cellulitis.

Rarely, in more severe cases, invasive GAS infections can cause osteomyelitis, endocarditis, and streptococcal toxic shock syndrome. Invasive GAS infection is pervasive across both developed and developing countries. Historically, the incidence of GAS disease is lowest in autumn, with rising incidence in December through April; this seasonality is thought to be due to prevalence of predisposing viral infections as well as climatic and behavioral changes, wherein children and adults spend more time indoors.<sup>7</sup> Classically, case fatality rates from invasive GAS infection in developed countries varied from 8% to 16%, with rates greater than 25% in developing countries,<sup>8</sup> and approaching 50% in the presence of streptococcal toxic shock syndrome.<sup>9</sup>

The virulent factors of GAS account for its ability to cause severe disease.<sup>8</sup> For example, the M protein allows GAS to evade phagocytosis by interfering with the complement arm of the immune system.<sup>10</sup> This protein also subsequently helps GAS invade sterile sites and ultimately with the aid of streptokinase, degrades surrounding tissues.<sup>11</sup> M protein as well as M-like protein and other adhesins allow GAS to colonize mucosal services.<sup>8</sup> Similar to other gram positive pathogens, such as *Staphylococcus aureus*, GAS produces exotoxins, e.g., streptococcal pyrogenic exotoxin A, that serve as superantigens.<sup>12</sup> This exotoxin stimulates T-cell activity by binding class II molecules on antigen-presenting cells to T-cell receptors, bypassing antigen processing and mounting cytokine release. Collectively, this leads to a toxic shock clinical presentation.<sup>13</sup> A hypervariable region of the M protein is encoded by the emm gene with different subtypes, and can be useful in differentiating GAS strains.<sup>14</sup> Over 25 emm types contribute to ~95% of GAS disease,<sup>8</sup> with preponderance of disease incidence caused by increases in emm1 or emm3.<sup>15</sup>

Nelson et al looked at epidemiologic trends for invasive GAS infection in the US from 2005 to 2012.<sup>16</sup> The annual incidence was highest among persons aged ≥ 65 years (9.4/100 000) or <1 year (5.3), and among blacks (4.7/100 000). National rates remained steady over the 8 years of surveillance. Factors independently associated with death included increasing age, recent surgery, septic shock, necrotizing fasciitis, meningitis, pneumonia, and underlying chronic illness or immunosuppression.

### An Increase in Invasive GAS Infections:

In 2020, Hollingsworth et al wrote about unintended outcomes of disease control measures as it pertains to endemic infections.<sup>17</sup> They termed this phenomenon as the “honeymoon effect” and its subsequent “divorce effect,” wherein the deployment of infection control measures may eventually engender a *larger* total number of infections. The authors showed that mathematical modeling explained the eventual increase in total number of infections as resulting from population-level losses of immunity. Studying the recent surge in iGAS infections, Aboulhosn et al, from Texas Children’s Hospital, extrapolated and applied this honeymoon and divorce phenomenon to the COVID-19 pandemic, surmising that, “unfortunately, the reduction or elimination of COVID-19 control measures had the unintended consequence of large outbreaks of non-COVID-19 infections due to exposure of a greater number of susceptible individuals.”<sup>18</sup> When masks and other mitigation measures were in place during COVID-19, it led to the decline of many other infections: the honeymoon effect. Unfortunately, the cessation of those measures led to a spike in non-COVID-19 infections: the divorce effect. Aboulhosn et al<sup>18</sup>

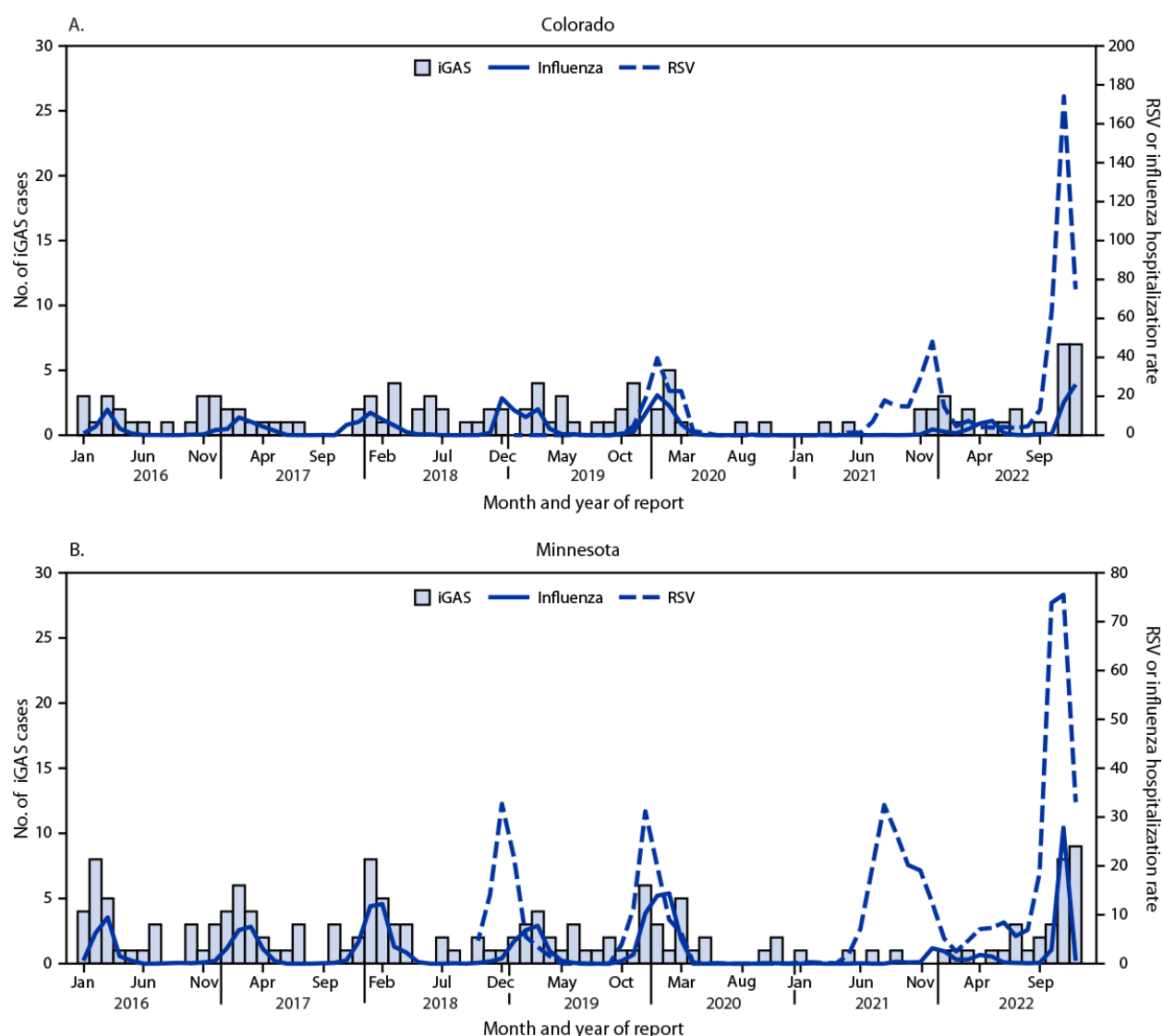




## Recent Increase in Invasive GAS Infections *Continued from Page 10*

also showed that, in 2022, out of 318 GAS cases, iGAS accounted for 31.4% with skin and soft tissue infections (SSTI) seen in 17.6%, and pharyngeal infections (PHG) in 50.9%. iGAS was more common among children less than 4 years. Comparing pandemic (2022) and pre-pandemic (2014–2018) data, authors showed a significant increase in iGAS cases in late 2022. Further, the emm12 GAS strain notably rose in 2022.

Another proposed mechanism for the increase in iGAS infections centers around synergy: underlying viral infections may create synergistic relationships with GAS, lending GAS the ability to better invade surrounding tissues.<sup>19</sup> In light of the recent COVID-19 pandemic, and disruptions to the normal circulation of respiratory viruses, one could postulate that SARS-CoV-2 and other respiratory viruses may also promote a synergistic effect with GAS. In a recent MMWR report, 62% of patients with invasive GAS had a preceding upper respiratory tract infection within 2 weeks of their invasive GAS infection.<sup>20</sup> In regard to the M protein gene typing results for strains causing invasive GAS disease during this surge, 35% were type emm1 and 50% were type emm12, both of which were noted to be the most common causes of invasive disease prior to this surge. No novel M protein types emerged to cause this uptick in disease incidence. Additionally, whole genome sequencing of isolates did not reveal changes to antibiotic susceptibility patterns.<sup>21</sup>

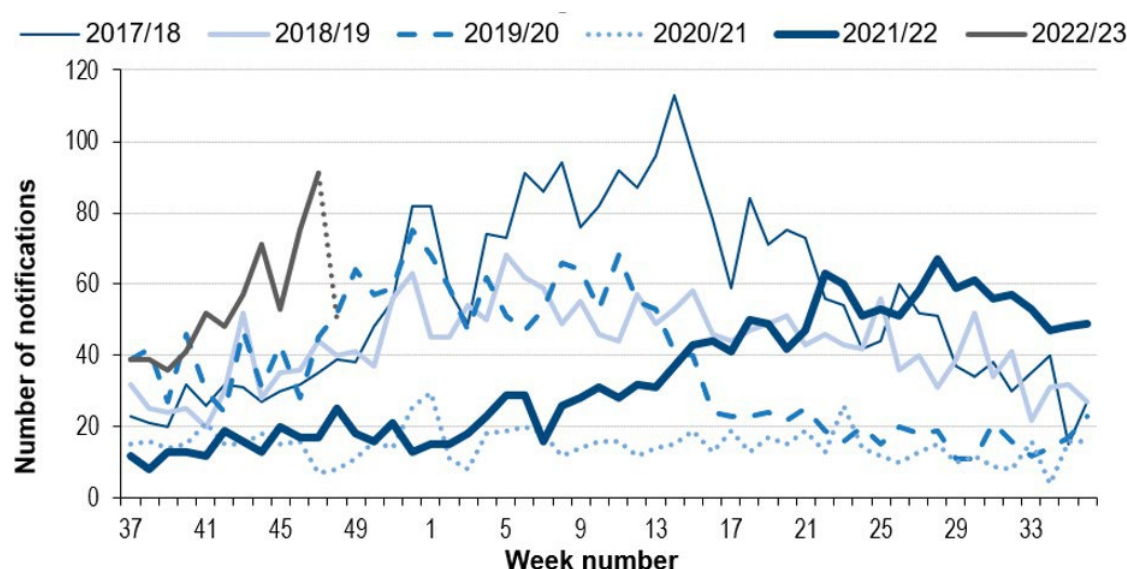


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## Recent Increase in Invasive GAS Infections Continued from Page 11

Cases of invasive group A *Streptococcus* infections and hospitalization rates for influenza and RSV among children and adolescents aged <18 years — Colorado and Minnesota, January 2016–December 2022. Image Source: *MMWR Morb Mortal Wkly Rep* 2023;72:265–267.

When researchers in the United Kingdom looked at iGAS infections from 2018 to 2022, they found that, historically, laboratory notifications of iGAS infections have predominantly been reported from blood culture specimens. From 2018–2022, 87% of iGAS infections were from blood specimens, and 5% from pleura and/or lower respiratory tract (LRT) specimens (17% in <15-year-olds). However, during the early part of the 2022/23 season, iGAS infections diagnosed from LRT specimens including pleural fluid specimens increased (12% of iGAS specimens in November 2022 for all ages; 44/365), particularly in children younger than 15 years (28% in November; 32/113).<sup>22</sup> Similarly in France, Lassoued et al<sup>23</sup> reported a dramatic increase in iGAS infections incidence related to various emm-types since October 2022. The increase in iGAS infections mainly involved pleural empyema cases and coincided with a major outbreak of respiratory viruses in the pediatric population.<sup>23</sup>



Weekly laboratory notifications of iGAS, England, by season, 2017 to 2018 onwards. Image Source: Group A streptococcal infections: first update on seasonal activity in England, 2022 to 2023. Updated 29 June 2023. <https://www.gov.uk/government/publications/group-a-streptococcal-infections-activity-during-the-2022-to-2023-season/group-a-streptococcal-infections-first-update-on-seasonal-activity-in-england-2022-to-2023>

### Going Forward:

*Streptococcus pyogenes* vaccine candidates apply both M protein and non-M protein based approaches. M protein-based vaccine candidates include StrepAnova, J8/S2 combivax, P\*17/S2 combivax, and StrepInCor; each demonstrating immunogenicity and safety in various trials.<sup>24</sup> Non-M protein vaccine candidates encompass Combo4, VAX-A1, Combo5, and TeeVax, targeting a range of antigens. These vaccine candidates offer potential broader coverage across *S. pyogenes* strains. Preclinical studies have shown varying degrees of protection against infections. The Strep A Vaccine Global Consortium (SAVAC) aims to accelerate *S. pyogenes* vaccine development by addressing knowledge gaps and promoting collaboration.<sup>25</sup> Yet, further clinical trials and efforts are required for these vaccine candidates' development, and their eventual success or failure is yet to be determined.

Finally, concern for GAS resistance needs to be addressed. Despite the use for penicillin for decades, *S. pyogenes* remains universally susceptible to penicillin.<sup>26</sup> But, in 2020 Vannice et al reported on a Seattle community outbreak of GAS which identified two isolates with reduced susceptibility to ampicillin, amoxicillin and cefotaxime.<sup>27</sup> These isolates were found to have mutations with a T553K substitution within the Penicillin-Binding Protein 2x (PBP2x). In the 1980s, high-level resistance to beta-lactams in *Streptococcus*

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## Recent Increase in Invasive GAS Infections *Continued from Page 12*

*pneumoniae* infections was found, and isolated to point changes in a single amino acid in *S. pneumoniae* PBP2x.<sup>28</sup> The discovery of similar changes in the Seattle outbreak led to concerns that, at least in theory, similar resistance might one day arise to penicillin itself.<sup>29</sup>

**Commentary:** As the COVID-19 pandemic evolves into its endemic phase, we as pediatricians will see in the coming years if there is a commensurate reduction, or normalization, in the amount of iGAS infections. Perhaps the curve of iGAS infections will bend downward as population-level immunity increases, and the divorce effect abates. Perhaps we will find definitive evidence of the synergy which comes from the infectious nature of widespread viral pathogens with GAS. *Streptococcus pyogenes* has afflicted humans, especially children, for throughout history. The burden of its infection has filled the waiting rooms of pediatric practices and hospital wards. We still have a lot to learn.

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## ID Pearls and Other Gems-Mosquito borne infections 2023 (Arbo- to Zika Virus) – Not so rare recently

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**Case:** A fully immunized previously healthy 8-year-old presents with a 3-day highly-febrile flu-like illness (headache, myalgia, nonlocalized abdominal pain, fatigue, occasional chills). No tick bites or recent travel are reported but dozens of mosquito bites are noted. This presentation usually indicates a viral illness, e.g. an enterovirus, but could it be a mosquito borne infection?

**Background:** Fall seems a weird time to discuss mosquito borne diseases. But tell me if you heard this one – “this past three years have been worse than any in the past 80 years”. With increasingly extreme unstable weather, warmer temperatures and more standing water make fertile areas for intense/extended breeding seasons. More low-lying coastal or inland waterway areas now support mosquitoes that can carry arthropod borne viruses (arboviruses), malaria, Chikungunya virus and Zika virus for more months of the year, e.g. *Culex*,

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## ID Pearls and Other Gems-Mosquito borne infections 2023

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*Aedes* and *Anopheles spp.* No continental US state is safe from mosquito borne infections. In this discussion we will focus on selected mosquito borne infections acquired within US borders (endemic, aka autochthonous or not-travel-related) as opposed to imported (travel-related) not acquired within US borders.

**Arboviruses** Arboviruses include members of the Flaviviruses (West Nile Virus, Dengue Virus and St. Louis Encephalitis virus), Togaviruses (Eastern Encephalitis Virus, Western Encephalitis Virus and Venezuelan Encephalitis Virus), and California Serogroup Bunyaviruses (La Crosse Virus, Jamestown Canyon Virus and California Encephalitis Virus).

West Nile Virus (WNV): Even before intensifying recent climate changes, WNV has been the most common endemic mosquito borne infection since 2000 (peak years 2003 and 2012), with 200-1000 cases annually.<sup>1,2</sup> WNV was first imported to the east coast (~1999) where native mosquitoes (mostly *Culex spp.*) were capable of acquiring, carrying and transmitting WNV. WNV swept across the US from 2000-2003, killing millions of birds and being a threat to horses (there is an equine WNV vaccine). WNV is now endemic, with only Alaska and Hawaii spared to date. Per CDC, 455 WNV disease cases have been reported in 36 states so far in 2023 as of Late August, with 315 being neuroinvasive cases, much of the activity in the Midwest. Figure 1.

Clinically, WNV infections are mostly asymptomatic, with only 10-25% producing symptoms, ~1% progressing to neuroinvasive disease and 3-15% mortality among those with neuroinvasive disease. Mild WNV illness usually presents with fever, headache, myalgia, arthralgia, and/or rash. Signs of severe/neuroinvasive West Nile virus disease (1/150 symptomatic cases) include mental status changes, seizures, light sensitivity, neck stiffness, muscle weakness, or paralysis and are more likely in the elderly and those with diabetes, hypertension, chronic renal disease, cancer, or alcohol overuse. Mortality (3-15% of severe cases) is more frequent in immune suppressed patients.<sup>3</sup> No specific therapy is available.

California Serogroup Viruses (CSG) were the most frequent causes of endemic US mosquito borne infection before West Nile Virus (WNV) entered the US in 1999.<sup>4</sup> Most were pediatric and due to La Crosse virus (~70 symptomatic cases annually) with acquisitions in areas near the Mississippi and Ohio rivers, but sometimes in the upper Midwest. While most La Crosse virus infections are asymptomatic, symptomatic infections present mostly with flu-like symptoms (fever, headache, myalgias and/or nausea) with very few progressing to encephalitis with mental status changes and/or seizures; the case fatality rate is <1%. No specific therapy is available.

Dengue Virus: While most US-diagnosed dengue infections (aka, break bone fever) are acquired outside the continental US, US-acquired dengue is not infrequent in Puerto Rico or the US Virgin Islands, and in 2023 has been reported in Florida, Texas, Arizona and Hawaii. <https://www.cdc.gov/dengue/areaswithrisk/in-the-us.html>

Worldwide, dengue is the most common arbovirus infection. Clinically, first time dengue virus infections (there are four types) usually range from asymptomatic to a flu-like illness, whereas repeat infections can be more severe and even fatal. Overall, symptoms occur in ~25% of dengue infections. Severe dengue occurs in up to 5% of infections, can rapidly progress in just a few hours, and is a medical emergency.

There are three described phases to severe dengue. The *febrile phase*, the critical phase, and the convalescent phase. The febrile phase usually includes 2-7 days of sometimes biphasic fever along with extreme thirst, severe headache, myalgia, arthralgia, retro-orbital eye pain, pale cold skin, and macular/papular rashes. Erythema of face, mouth and throat can occur. Sometimes signs of abnormal bleeding occur (nosebleeds, petechiae, ecchymoses, purpura, gum bleeding, hematuria, and/or tourniquet test positivity).

The *critical phase* (usually lasting 24-48 hours) usually starts near defervescence with lethargy, postural hypotension, persistent emesis, severe abdominal pain, enlarging liver, shortness of air, and/or puffiness of face/extremities. Laboratory abnormalities may include rising hematocrit, leukopenia, thrombocytopenia, hyponatremia, elevated liver enzymes, in the face of a normal erythrocyte sedimentation rate. While most patients improve during the critical phase, signs of fluid third spacing can be harbingers of progression (narrowing pulse pressures, pleural effusion, ascites, further increased hematocrit, hypoproteinemia and shock). Despite early shock, these patients can appear deceptively less ill than they are, but then quickly crash into irreversible shock and death. Patients can also develop hemorrhagic signs (hematemesis, bloody stool, or menorrhagia). Less often pancreatitis, hepatitis, myocarditis or encephalitis may occur.

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## ID Pearls and Other Gems-Mosquito borne infections 2023.....Continued from Page 15

Those who survive to the *convalescent phase* gradually undergo diuresis and reabsorb third spaced fluid producing improved blood pressure (perhaps with temporary bradycardia) along with dropping (normal or low) hematocrit and rising platelet count. Existing rashes can become pruritic and then peel.

There is no specific treatment, but fluid replacement can be critical; treating pain is important usually with acetaminophen because non-steroidal anti-inflammatory drugs or aspirin can increase the risk of bleeding. Patients with platelet counts  $<20,000/\text{mm}^3$  are at high risk of severe bleeding requiring emergent platelet transfusions. A Dengue vaccine has recently become available for selected children <https://www.cdc.gov/vaccines/vpd/dengue/public/index.html>, i.e. (9-16 year olds known to be previously infected and residing in endemic areas).

**Viral Disease Considerations:** Other than WNV and with recent travel histories, providers outside of Puerto Rico and certain semi-tropical US areas have had comfort knowing that undifferentiated febrile illnesses are not mosquito borne. That said, a few CSG viral infections occur sporadically or intermittently in different regions mostly in summer, with the viruses usually having selected US regions of activity. For example, this year Jamestown Canyon virus (JCV) was reported in Michigan (less than a dozen cases). Select regions are also at risk for St. Louis encephalitis, Eastern equine and Western Equine encephalitis virus. In North America, La Crosse and JCV are the main disease-causing endemic CSG viruses.

**Malaria .** Malaria is a reportable disease (<https://www.cdc.gov/malaria/report.html>) and is the most common mosquito borne infection worldwide (~230 million annually) Malaria is rare in the US (~2,000 cases per year); almost all cases are travel-related. Malaria is usually transmitted via infected female *Anopheles* mosquitoes ( $<1\%$  of US cases are via blood products). The two forms acquired in the US are due to *Plasmodium* (*P.*) *vivax* and *P. falciparum*. *P. falciparum* causes more severe infections and is also more common (3:1) worldwide, so imported cases are also mostly *P. falciparum*. However, the 2023 endemic US cases (the first since 2003) are mostly *P. vivax* (Florida 7 cases and Texas 1 case) vs. *P. falciparum* (Maryland 1 case). Note: WHO declared the US malaria-free in 1970.

Children, pregnant persons, and immune suppressed persons are at highest risk for severe malaria. Fever (often with a pattern of relapsing episodes with *P. vivax*) is a hallmark and the most common malaria symptom. But headache, nausea, vomiting, abdominal pain, diarrhea, cough, and myalgia/arthralgias are frequent with uncomplicated malaria. Signs/symptoms heralding severe malaria include: difficulty breathing, organ failure, altered consciousness, seizures, and/or severe anemia. While liver and red blood cells are the factories for malaria organism production, toxic effects can occur in any organ system.

Direct microscopy of three blood smears is a classic diagnostic tool but rapid diagnostic tests (RDT) are often used for screening. Microscopy is more sensitive than RDT and is needed to distinguish among malaria species and determine parasite load (necessary for appropriate treatment). PCR testing is also possible but not commercially available. Treatment differs for *P. vivax* vs. *P. falciparum*, and for children vs. adults, with special considerations for pregnant persons and regimens are based on the patient's parasite being chloroquine resistant or not. (<https://www.cdc.gov/malaria/about/biology/index.html>) Also, *P. vivax* infections require 2-step regimens to prevent relapses.

**Caution:** We need to consider mosquito borne infections even late in the year in most US locales, given the mildness of winters and mosquitoes being seen during most months as far north as the Canadian border. This is not totally new, considering the rising concern as early as 2019 of increasing numbers of disease carrying mosquitoes and the expanding areas of where they are found<sup>5</sup>.

**Next step when reasonable suspicion exists:** Reviewing diagnostics and management including all the nuances of test interpretation is beyond the scope of this article. The bottom line is that, particularly in areas with recently reported mosquito borne diseases, consultation with local health departments or infectious disease specialists will ensure timely and optimum workup, including rapid initiation of therapy if malaria is indeed the cause.

Takeaway general facts about mosquito borne viral disease:

1. Mosquito borne infections are not directly contagious person-to-person.
2. Most mosquitoes in the US do not carry a pathogen even in pathogen-endemic areas.
3. Most persons infected with mosquito borne viruses do not become symptomatic.

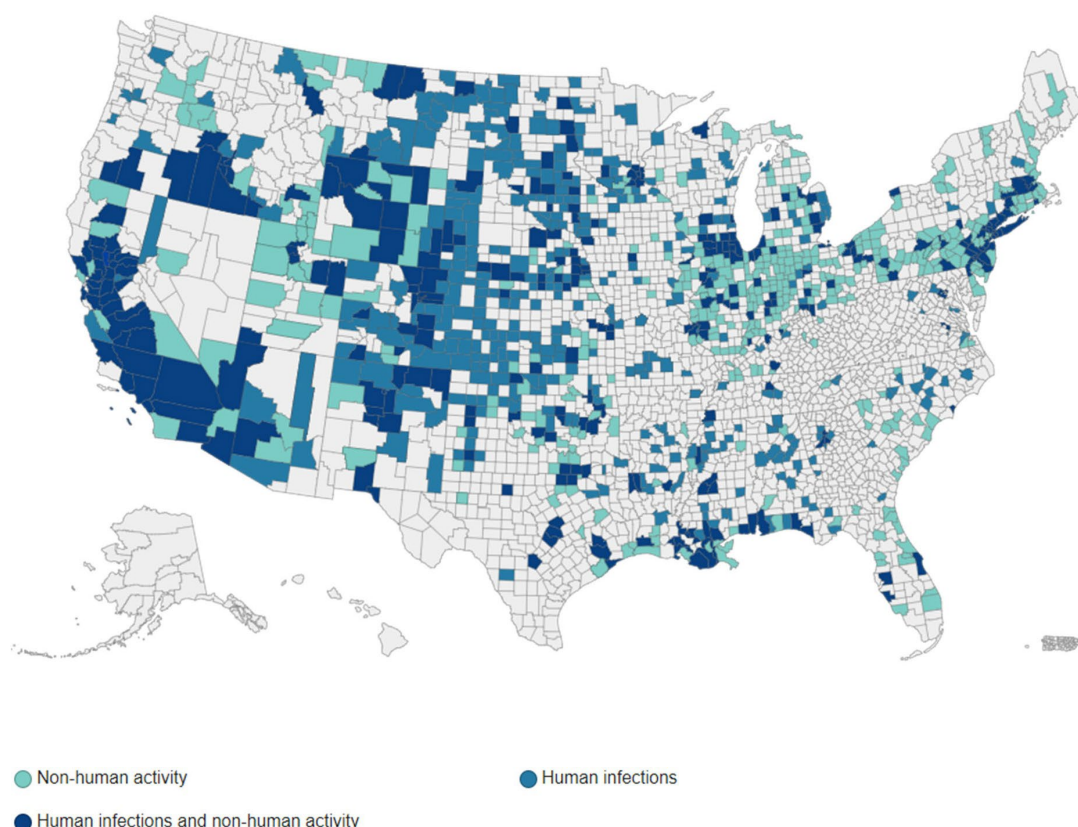
Continued on Page 17

**D Pearls and Other Gems-Mosquito borne infections 2023***Continued from Page 16*

4. Most symptomatic infections are not severe or neuroinvasive.
5. Public health groups are now concerned that Zika and Chikungunya infections may become regular events in the US.

Final note on malaria: Of US mosquito borne infections, only malaria has a pathogen-specific treatment. Early diagnosis/treatment is critical to limit/cure disease in the infected person. Moreover, clearing parasitemia will also restrict further spread of the pathogen into new mosquito vectors pools.

**Figure 1** West Nile Virus activity in the US as of the end of August 2023



Non-human activity: Veterinary disease cases or infections in mosquitoes, birds, or sentinel animals have been reported to CDC.

Human infections: Human disease cases or infections in blood donors reported to CDC.

Human infections plus non-human activity: Both human infections and non-human infections.

Source: <https://www.cdc.gov/westnile/statsmaps/current-season-data.html>

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## Review of the Recent Infectious Diseases Literature

**Publication:** Strasser S, Relly C, Berger C, Trück J. Structured immune workup in healthy children with a first episode of severe bacterial infection: a 7-year single-center study. *The Journal of Infectious Diseases* 2023; 228: 8-17.

**Reviewed by:**

Jane M. Gould, MD, Medical Epidemiologist, Healthcare-Associated Infections/Antimicrobial Resistance Program, Division of Disease Control, Philadelphia Department of Public Health, Philadelphia, PA

**Accompanying editorial commentary:** Bijker EM, Van Well GTJ. Immunological evaluation of children with a first severe bacterial infection: standard of care? *The Journal of Infectious Diseases* 2023; 228: 1-3.

Sepsis is a leading cause of death and disability in children. Globally more than one million childhood deaths per year are secondary to sepsis. Each year more than 75,000 children in the U.S. develop severe sepsis and approximately 7,000 of these will die.<sup>1</sup> Childhood sepsis deaths are estimated to occur in 35%-50% of previously healthy infants despite access to vaccination, health care, and effective antibiotics.<sup>2-5</sup> Previously, primary immunodeficiency as a risk factor for sepsis was thought to be extremely rare and guidance to recommend immunologic or genetic investigations after a first sepsis episode do not currently exist.<sup>6-8</sup> Early recognition of immune disorders after a first episode of severe bacterial infection could prevent deaths and disability; such as amputations, brain damage, learning difficulties and hearing loss by initiating prevention strategies such as prophylactic antimicrobials and vaccines as well as providing heightened caregiver and healthcare professional awareness for rapid initiation of medical evaluation and empiric antimicrobials.

Investigators from the University Children's Hospital of Zurich conducted a retrospective, single center, cohort study of previously healthy children aged 3 days to 18 years old who were admitted with severe bacterial infections (SBI) including pleuropneumonia (PP), meningitis and/or sepsis over a 7-year time-period. Beginning in 2013 this hospital began routinely conducting immunological testing of all previously healthy children presenting with proven or clinically diagnosed SBI. Definitions used for this study were as follows: PP was severe pneumonia with pleural effusion on radiograph or sonograph; bacterial meningitis was a positive cerebrospinal fluid culture or presence of clinical and laboratory features consistent with bacterial meningitis; and sepsis was a case of isolated bacteremia with clinical signs of sepsis or septic shock in the context of a proven or suspected bacterial infection. Children with other SBI, including cases of bacteremia with urinary tract infections or osteomyelitis, as well as early onset sepsis (onset <3 days of life) and viral, fungal, *Borrelia* or mycobacterial infections were excluded. Children with underlying co-morbid conditions with increased susceptibility to infection, anatomic abnormalities, medical device-associated or healthcare associated infections, recent trauma or burns were also excluded. Immune system testing included: absolute neutrophil count (some patients also had neutrophil function testing using dihydrorhodamine [DHR]/nitroblue tetrazolium [NBT]), assessment of classic and alternative complement pathway activity, total immunoglobulin concentrations (IgG, IgA, IgM), specific antibodies against polysaccharides and proteins contained in vaccines, pitted erythrocytes (as a marker for functional asplenia) and less often lymphocyte phenotyping by flow cytometry. An inborn error of immunity (IEI) was defined as single or repetitive low IgG concentrations in patients > 3 months of age, repetitive and inadequately low specific antibodies against vaccine antigens in children despite vaccination (specific antibody deficiency), genetically confirmed complement deficiency or functionally confirmed autoimmune neutropenia. Transient hypogammaglobulinemia of infancy was defined as repetitive low IgG with or without IgA/IgM deficiency with documented normalization over time.

Of the 432 children with SBI, findings could be analyzed in 360. Follow-up data was available for 265 (74%), of whom 244 (92%) underwent immunological testing and 21% of those had laboratory abnormalities. Fourteen children (6%) had an IEI considered clinically relevant (3 complement deficiencies, 1 autoimmune neutropenia, 10 humoral immunodeficiencies) and 27 (11%) had milder humoral abnormalities or findings suggestive of delayed adaptive immune maturation. The IEI percentage was even higher for patients with sepsis or septic meningitis and in those aged < 1 year old compared with the entire follow-up cohort. Isolation of *Streptococcus pneumoniae* (most often PCV-13 serotypes 69%) was the most common bacteria from all three SBI phenotypes followed by *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Neisseria meningitidis* and *Hemophilus influenzae*. Of the 27 patients with SBI caused by PCV-13 serotypes, 41% were fully vaccinated according to Swiss vaccination schedules including PCV13, 15% were vaccinated with PCV-7 only, and 44% had incomplete or unknown vaccine status. Meningococcal serogroup B was most frequently detected of all grouped meningococcal isolates and *H. influenzae* had equal proportions of type b and non-typeable. Vaccination status against *N. meningitidis* and *H. influenzae* was not reported.

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## Review of the Recent Infectious Diseases Literature *Continued from Page 18*

This study revealed a significant percentage (6%) of previously healthy children with SBI had impaired immune function and a further 11% had milder humoral abnormalities or findings suggestive of delayed adaptive immune maturation. Children <1 year old and those presenting with sepsis or septic meningitis had a 2-fold higher chance of having abnormal immune laboratory testing or being diagnosed with an immunodeficiency. Additionally, children with PP without sepsis had the lowest rates of immunological abnormalities. The limitations of this investigation included its retrospective study design which could have introduced bias, results are from a single center where the racial and ethnic diversity of the patient population was not addressed, and the potential for under identification due to patient exclusions and the non-standardized limitations of immune testing. The results suggest that screening children for immunological abnormalities after a SBI, especially after bacterial meningitis and sepsis, would allow for early identification and use of preventative measures. The issue of exactly who to test, what tests to use, and when best to test will require further study including multicenter prospective investigations with cost effectiveness analyses. An accompanying commentary points out that an expert consensus panel and standardized prospective data collection would ultimately be needed to address these questions.

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## New ID Policies/Guidelines

*Andrea Sperduto, MD, FAAP, Cleveland Clinic Foundation, Cleveland, OH*

### I. MMWR

- a. Interim Recommendations for Use of Bivalent mRNA COVID-19 Vaccines for Persons Aged >6 months- United States, April 2023. June 16, 2023. MMWR:72(24);657-662.  
<https://www.cdc.gov/mmwr/volumes/72/wr/mm7224a3.htm>
  1. October 2022, CDC recommended a bivalent COVID-19 mRNA vaccine dose for all persons aged >5 years who had received a monovalent primary vaccination series.
  2. December 2022, CDC recommended single dose bivalent vaccine for children aged 6mos- 4yrs as 3rd dose in primary series.
  3. March 2023, CDC recommended single dose of bivalent vaccine for children aged 6mos- 4yrs who rec'd 3 monovalent doses for primary series.
  4. April 2023, CDC recommended:

*Continued on Page 20*

**New ID Policies/Guidelines** *Continued from Page 19*

1. A single bivalent vaccine dose for most persons aged >6 years,
2. Bivalent vaccines for children ages 6mos- 5 years,
3. Optional additional bivalent booster doses for moderately or severely immunocompromised persons aged >6mos if last bivalent was >2mos earlier and for those > 65 years if last bivalent dose was > 4mos earlier.
- b. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices- United States, 2023. July 21, 2023. MMWR:72(29);792-801.  
<https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm#suggestedcitation>
  1. May 2023, FDA approved the first two vaccines for prevention of RSV lower respiratory tract disease (LRTD) for use in adults aged >60 years.
    - i RSVPreF3 (Arezvy, GSK)- a 1-dose adjuvanted (ASO1E) recombinant stabilized prefusion F protein (preF) vaccine.
    - ii RSVpreF (Abrysvo, Pfizer)- a 1- dose recombinant stabilized preF vaccine.
    - iii June 21, 2023, ACIP recommended that persons aged >60 years may receive a single dose of RSV vaccine with shared clinical decision making.
    - iv Available data on immunogenicity of co-administration of RSV vaccines and other vaccines are currently limited.
- c. Use of Nirsevimab for the Prevention of Respiratory Syncytial Virus Disease Among Infants and Young Children: Recommendations of the Advisory Committee on Immunization Practices- United States, 2023. August 25, 2023. MMWR:72(34);920-925.  
<https://www.cdc.gov/mmwr/volumes/72/wr/mm7234a4.htm>
  1. ACIP recommended as of August 3, 2023.
  2. Infants aged <8 mos born during their first RSV season should receive one dose of nirsevimab RSV monoclonal antibody (Beyfortus, Sanofi and AstraZeneca) (50 mg for infants <5 kg and 100 mg for infants >5 kg.
  3. Children aged 8-19 mos who are at increased risk of severe RSV disease (e.g. chronic lung disease who requires medical support, children with severe immune suppression, children with cystic fibrosis under certain circumstances, American Indian or Alaska Native children) and entering their second RSV season should receive 1 dose of nirsevimab (200 mg).
- d. Prevention and Control of Seasonal Influenza with vaccines: Recommendations of Advisory Committee on Immunizations Practices- United States, 2023-24 Influenza Season. August 25, 2023. MMWR:72(2);1-25.  
<https://www.cdc.gov/mmwr/volumes/72/rr/rr7202a1.htm>
  1. All persons >6 mos with egg allergy should receive influenza vaccine. ANY influenza vaccine (egg based or non-egg based) that is otherwise appropriate for the recipient's age and health status can be used.
  2. All vaccines are quadrivalent, containing hemagglutinin derived from one influenza A(H1N1)pdm09 virus, one influenza A (H3N2) virus, one influenza B/Victoria lineage virus, and one influenza B/Yamagata lineage virus.

**II. IDSA**

- a. IDSA 2023 Guidance on the Treatment of Antimicrobial Resistant Gram-Negative Infections. Published by IDSA, Clin Inf Dis, 7/18/23.  
<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciad428/7226183?login=false>
  1. Treatment of infections caused by the following bacteria:
    - i Extended-spectrum *B-lactamase*-producing *Enterobacterales* (ESBL-E).
    - ii AmpC B-Lactamase-producing *Enterobacterales* (AmpC-E).
    - iii Carbapenem-resistant *Enterobacterales* (CRE).
    - iv *Pseudomonas aeruginosa* with difficult-to-treat resistance (DTR-*P. aeruginosa*).
    - v Carbapenem-resistant *Acinetobacter baumannii* species (CRAB).
    - vi *Stenotrophomonas maltophilia*.
- b. Hepatitis C Guidance 2023 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. Clin Inf Dis, 5/25/2023. <https://academic.oup.com/cid/advancearticle/doi/10.1093/cid/ciad319/7179952?login=false>
  1. Last developed in 2013 but updated in 2020.
  2. This update focuses on changes to the guidance from the previous 2020 version.
  3. Updated treatment and retreatment recommendations for children as young as 3 years of age.
- c. Infectious Diseases Society of America Guidelines on the Treatment of Patients with COVID-19.  
<https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>
  1. Updated regularly when new information is released.
  2. Last updated June 26, 2023.

*Continued on Page 21*

**New ID Policies/Guidelines** *Continued from Page 20***III. HIV GUIDELINES**

Complete guidelines and information can be found at: <https://clinicalinfo.hiv.gov/en/guidelines> as are updated periodically.

Some of the highlights are listed below:

- a. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection.
  1. Last updated April 11, 2023.
  2. The section on “When to start ART” has been defined as “Therapy initiated immediately or within days of HIV diagnosis” with some specific exceptions (cryptococcal meningitis, disseminated Mycobacterium avium Complex Disease, or Mycobacterium tuberculosis).
  3. Updates in regimens for children with sustained virologic suppression.
  4. Updates regarding infant feeding for individuals with HIV in the United States. (Same information is given under “use of ARV in pregnant people” below).
- b. Recommendations for the Use of ARV Drugs in Pregnant People with HIV Infections and Interventions to Reduce Perinatal HIV Transmission.
  1. Last updated January 31, 2023.
  2. Use of long-acting cabotegravir (CAB) as PrEP may be initiated or continued in pregnant people.
  3. Recommendations for the use of antiretroviral drugs during pregnancy was reorganized and revised.
  4. New section added about the use of ARV drugs before and during pregnancy to improve maternal health and prevent perinatal HIV transmission (including ARV’s for HIV exposed newborns).
  5. New section on people with HIV who are trying to conceive.
  6. Newly titled section: “Infant Feeding for Individuals with HIV in the United States”. (Can also find this section in “Guidelines for Use of ARV Agents in Pediatric HIV Infection”).
    - i. Replacement of feeding with properly prepared formula or pasteurized donor human milk from a milk bank eliminates the risk of postnatal HIV transmission to the infant.
    - ii. Achieving and maintaining viral suppression through ART during pregnancy and postpartum decreases breastfeeding risk to less than 1% but NOT zero.
  - iii. Replacement feeding with formula or banked pasteurized donor human milk IS recommended to eliminate risk of HIV transmission in those people who are not on ART and/or do not have a suppressed viral load during pregnancy and delivery.
  7. Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection.
    - i. When criteria for low risk perinatal HIV transmission are met, infants should receive 2 weeks of zidovudine (ZDV) prophylaxis rather than 4 weeks.
    - ii. Infants who do not meet criteria for low risk but have viral load <50 copies/mL at or after 36 weeks should receive ZDV for 4-6 weeks.
    - iii. Newborns at high risk of perinatal acquisition, should receive 3-drug regimens from birth for 2-6 weeks. If the duration of the 3-drug regimen is shorter than 6 weeks, ZDV should be continued alone to complete total of 6 weeks of prophylaxis.
    - iv. All premature infants <37 weeks gestation who are not at high risk, should receive ZDV for 4-6 weeks.
  8. Diagnosis of HIV Infection in Infants and Children.
    - i. Section provides additional guidance on HIV diagnostic testing for infants with perinatal HIV exposure who are being breastfed.
- c. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV.
  1. Last updated March 23, 2023
  2. Lenacapavir, a first-in-class HIV capsid inhibitor, was approved by FDA December 2022 to be used in combination with other ARV drugs for treatment of heavily treatment-experienced adults with multidrug-resistant HIV-1 infection.

## Policy highlights from the AAP Committee on Infectious Diseases (COID)

**The COID published the following statements over the past six months:**

1. Technical Report - Palivizumab Prophylaxis in Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection
2. ACIP and AAP Recommendations for Nirsevimab
  - a. Related News and Education:
    - i. Pediatrics On Call Podcast: Immunizations Special: RSV, COVID, Pneumococcal Disease, Influenza
3. Recommendations for Prevention and Control of Influenza in Children, 2023-2024, were released online on August 29th and will be published in the October edition of Pediatrics:
  - a. Policy Statement: <https://doi.org/10.1542/peds.2023-063772>
  - b. Technical Report: <https://doi.org/10.1542/peds.2023-063773>
  - c. Related News and Education:
    - i. COCA Call: AAP & CDC 2023-2024 Recommendations for Influenza Prevention & Treatment;
    - ii. HealthyChildren.org: The Flu: What Parents Need to Know (available in multiple languages)
    - iii. Red Book® Online Webinar: Pandemic Influenza Preparedness
    - iv. AAP.org/influenza: How to Set Up a Flu Clinic; Flu Toolkit with Graphics, Videos, Social Media Posts, and Sample Emails; Pandemic Influenza Information and Resources

**The following statements are in progress** (CR = clinical report, PS= policy statement, TR = technical report):

### a. New Intents

1. Intent to revise CR: Infectious Diseases Associated with Organized Sports and Outbreak Control (working on the intent)
2. Intent to revise PS: Cochlear Implants in Children: Surgical Site Infections and Prevention and Treatment of Acute Otitis Media and Meningitis (working on the intent)
3. Intent to revise TR: Immunizing Parents and Other Close Family Contacts in the Pediatric Office Setting (w/ Committee on Practice and Ambulatory Medicine, working on the intent)

### b. Statements in Progress

1. Revision of CR: Infection Prevention and Control in Pediatric Ambulatory Setting (first draft)
2. Revision of PS: Medical Versus Nonmedical Immunization Exemptions for Child Care and School Attendance (w/ Committee on Practice and Ambulatory Medicine, Council on School Health, Committee on State Government Affairs, working on first draft)
3. Revision of CRs: The Need to Optimize Adolescent Immunization and Practical Approaches to Optimize Adolescent Immunization (working on revising)
4. Revision of CR: Strategies for Prevention of Health Care-Associated Infections in the NICU (w/ Committee on Fetus and Newborn, working on the first draft)
5. New CR on Strategies for the Prevention and Management of Invasive Candida Infections in the NICU (w/ Committee on Fetus and Newborn, working on the first draft)
6. New CR on Antibiotic Stewardship in the NICU (w/ Committee on Fetus and Newborn, working on the first draft)
7. Revision of PS: Medical Countermeasures for Children in Public Health Emergencies, Disasters, or Terrorism (w/ Council on Children and Disasters, working on the first draft)
8. Revision of CR: Strategies for Improving Vaccine Communication and Uptake (w/ Committee on Practice and Ambulatory Medicine and Committee on Bioethics, submitted to BOD)
9. New CR: Care of the Infant Exposed Congenitally to Cytomegalovirus (CMV) (w/ Committee Fetus and Newborn, Council on Children with Disabilities, Section on Otolaryngology-Head and Neck Surgery, working on the first draft)
10. New CR: Oral vs. Intravenous Antibiotic Therapy for Serious Pediatric Infections (w/ the Committee on Hospital Care, working on first draft)
11. Revision of TR: Non-Therapeutic Use of Antibiotics in Animal Agriculture: Implications for Pediatrics (w/ Council on Environmental Health and Climate Change, post review by internal and external stakeholders)
12. New CR: Fecal Microbiota Transplantation (FMT): Guidance for the Pediatrician (w/ Section on Gastroenterology, Hepatology and Nutrition, approved for publication)



## Red Book 2024

The development of the *Red Book 2024* is well underway. The editorial team for this edition is David Kimberlin, MD, FAAP, Editor, and Associate Editors Ritu Banerjee, MD, PhD, FAAP, Elizabeth Barnett, MD, FAAP, Ruth Lynfield, MD, FAAP, and Mark Sawyer, MD, FAAP. The chapters are currently being reviewed by the Board reviewers. The 33rd edition of the Red Book will be published in the spring of 2024.

Please send any questions to Gillian Gibbs, MPH, Senior Manager, Infectious Diseases Policy and Programs [ggibbs@aap.org](mailto:ggibbs@aap.org).

## Red Book Online — Celebrating 20 Years

Jennifer McDonald, Senior Editor, Digital Publishing, AAP

Since its first publication in 1938, Red Book continues to be the authority on pediatric infectious diseases from the American Academy of Pediatrics (AAP). Launched in 2003, Red Book Online (RBO) not only includes the current edition of Red Book but also instant access to the most reliable and clinically relevant content on childhood infectious diseases, making it the quickest and easiest way to keep pace with the latest developments and clinical guidelines. Use RBO anywhere, anytime. AAP Members receive access to [Red Book Online](#) as a member benefit.

“RBO deftly shares the tradition of excellence as the ‘latest and greatest’ definitive source for child health professionals to get all the answers they need at point-of-care to treat, manage and prevent infectious diseases in children, using the best available evidence gathered by the AAP.”

—David W. Kimberlin, MD, FAAP, Red Book editor since 2012

### Red Book Then

In celebration of the 20th anniversary of Red Book Online, we reflect on the first edition of the Red Book published in 1938—a mere 8 pages covering a mix of 18 topics. Look back at the original [1938 Red Book chapter “Epidemic Parotitis”](#) to read more about the chapter’s evolution from just 7 lines of text to 6 pages delineating etiology, epidemiology, diagnostics, and prevention by vaccination.

### VI. EPIDEMIC PAROTITIS

A. **Test:** None. B. **Active Immunity:** None. C. **Passive Immunity**—1. **Treatment:** Convalescent serum has been used in doses of from 50 cc. to 100 cc. and is injected intramuscularly to prevent complications. There is no definite proof that it will prevent complications. 2. **Exposures:** From 6 cc. to 10 cc. of convalescent serum have been given intramuscularly, but there is no evidence that it has any value.

### Red Book Now

The AAP *Red Book* is published every three years, but the pediatric infectious disease landscape is changing continuously. *Red Book Online* is consistently updated with the latest recommendations from the AAP. This approach ensures that pediatric healthcare professionals have access to the most current information, enabling them to deliver optimal care to children.

The revised and updated [Red Book: 2021–2024 Report of the Committee on Infectious Diseases, 32nd Edition](#) on RBO is the easiest way to find infectious disease information. Use the new split-screen functionality to view Red Book chapter text and figures, images, tables, references, and related content side by side. Use the left side navigation to jump directly to chapter sections and take advantage of fully embedded links within these sections to quickly view supporting content.

As part of RBO’s commitment to ensuring the most current information for pediatricians, the [ACIP and AAP Recommendations](#) on the use of Nirsevimab, a long-acting monoclonal antibody product intended for use in newborns and infants to protect against respiratory syncytial virus disease, was published in August 2023 on RBO shortly after approval by the US Food and Drug Administration and

*Continued on Page 24*

## Red Book Online — Celebrating 20 Years *Continued from Page 23*

Centers for Disease Control and Prevention (CDC).

Additionally, since the current edition published in June 2021, the following chapters were updated in *Red Book Online*: [Cholera](#), [Dengue](#), [Human Immunodeficiency Virus Infection](#), Rabies, Streptococcus pneumoniae (Pneumococcal) Infections, and Tuberculosis. View current updates on the [Updates and Errata](#) page.

### Getting the Most from RBO—Your AAP Member Benefit

Systems-based Treatment Table on Your Mobile Device

*Red Book Online*'s most-used resource, the Systems-based Treatment Table, is now available in a new mobile view that makes it easy to use on your phone or tablet. Just visit the **Systems-based Treatment Table** and “Switch to Mobile-Friendly View.” Don't forget to use your device's “Add to Home Screen” feature to save the mobile view of this table to your home screen for fast access.

### Outbreaks

Find information on the latest infectious disease outbreaks with [Red Book Online Outbreaks](#). Overseen by members of the AAP Committee on Infectious Diseases (COID), this [section](#) provides health care professionals with a quick resource to get up to speed on current outbreaks that have been identified in multiple US states and that affect the pediatric population. While this section primarily focuses on infectious outbreaks in the United States, other outbreak types may be covered occasionally as situations warrant.

### Influenza News and Resources

Compiled by the AAP COID, [Influenza News and Resources](#) provides a comprehensive list of information and resources on influenza prevention and treatment in children and adolescents. With flu season quickly approaching, this page will be continuously updated to include the most recent influenza information from the AAP and CDC, including the just published AAP [policy statement](#) and [technical report](#) “Recommendations for Prevention and Control of Influenza in Children, 2023-2024.”

### Webinars

*Red Book Online* Webinars include [presentations](#) from distinguished experts on important and timely topics in pediatrics. See the new RBO Webinar [Pandemic Influenza Preparedness](#) by Tim Uyeki, MD, MPH, MPP, FAAP. In this webinar, Dr Uyeki, Chief Medical Officer within the CDC Influenza Division's Office of the Director, provides an overview of what pandemic influenza is and how pediatric practices can prepare. This short webinar covers past influenza pandemics, the origin of pandemic influenza viruses, the impact of pandemic influenza on children, treating and preventing the spread of influenza, and preparing for pandemic influenza.

If you missed it, be sure to view the RBO Webinar [Planning for the Next Influenza Season: Pre-Booking](#) for an overview on what to consider when pre-booking influenza vaccines, such as reviewing vaccine manufacturer policies and considering lessons learned from the current influenza season to inform what vaccines to order for the next season.

### Vaccine Status Tables

The following three [Vaccine Status Tables](#) on RBO are continually updated with the latest information about recently submitted, licensed, and recommended vaccines and biologics, including status of the US Food and Drug Administration licensure process and related AAP and CDC recommendations. Try the “Mobile View” of the tables for easier use on your phone or tablet.

- **Table 1:** Status of Recently Submitted, Licensed, and Recommended Vaccines & Biologics
- **Table 2:** Status of Recently Submitted, Licensed, and Recommended Influenza Vaccines
- **Table 3:** Sars-CoV-2 Vaccines

### News

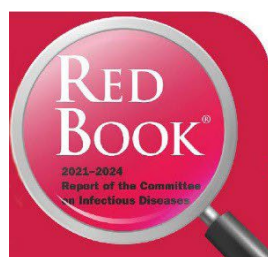
Check the [News](#) page often for breaking news related to pediatric infectious diseases and immunizations, including content updates, new vaccine recommendations, vaccine or antiviral shortages, disease outbreaks, and more.

Help us celebrate 20 years of *Red Book Online*! Read more about this exciting milestone in the AAP News article [Red Book Online marks 20 years as must-have pediatric infectious diseases resource](#).

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**Red Book Online — Celebrating 20 Years** *Continued from Page 24***We Want Your Feedback!**

Questions, comments, suggestions about *Red Book Online* can be submitted at <https://www.aap.org/RBOfeedback>

**Diagnosis Detective—New Feature on RBO!**

# Diagnosis Detective

**Can you solve it?**

[Diagnosis Detective](#) is an exciting new feature on *Red Book Online* (RBO) that challenges you to solve a new infectious disease case every month. Developed by a dedicated subteam of the COID, this new feature offers the following benefits:

- **Monthly Diagnostic Challenge:** Return monthly to test your diagnostic skills with new infectious disease content and images.
- **Interactive Quiz:** Actively participate and learn by solving real-world infectious disease cases.
- **Teaching/Learning:** Use the valuable infectious disease educational content in this new feature to learn, as well as reference as needed.
- **Social Sharing:** Share your success on social media platforms—Facebook, LinkedIn, and Twitter/X.
- **Archived Cases:** Challenge yourself with previous cases, which will be archived, for continued learning or if you missed a previous month's case.

Solve this month's infectious disease case at <https://publications.aap.org/redbook/resources/24128>.

**November 1, 2023: Red Book Online Chapter Update—[Streptococcus pneumoniae \(Pneumococcal\) Infections](#)**

The [Streptococcus pneumoniae \(Pneumococcal\) Infections chapter](#) in Red Book on Red Book Online was just updated to reflect the updated guidelines for the use of a new 20-valent pneumococcal conjugate vaccine (PCV20, Prevnar 20, Pfizer) for children.

Summary: On September 29, 2023, the Centers for Disease Control and Prevention (CDC) published updated guidelines for the use of a new 20-valent pneumococcal conjugate vaccine (PCV20, Prevnar 20, Pfizer) for children. The CDC recommends use of PCV20 as an option to PCV15 for:

- Routine vaccination of all children aged 2–23 months;
- Catch-up vaccination for healthy children aged 24–59 months who have not received age-appropriate doses; and
- Children aged 24–71 months with certain underlying medical conditions at increased risk for pneumococcal disease who have not received age-appropriate doses.

See the full update in the [Streptococcus pneumoniae \(Pneumococcal\) Infections chapter](#) in Red Book on Red Book Online.

## Welcome to New SOID Members!

If you know of others who might be interested in joining the Academy and the Section please have them call AAP Customer Services at: 866-843-2271 or visit [www.aap.org](http://www.aap.org) and click on the “Become A Member” link in the upper righthand corner of the page. Current Academy members may join the Section [here](#) (member ID and login required).

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