Between the end of August and through the fall of last year, several of you contacted me about cases of atypical hand foot mouth syndrome (HFMS). In most cases, physicians had noted the lesions and course seemed to be unusually severe. A recent publication from the CDC may shed some light on these cases.1

**Typical HFMS:** Outbreaks of Coxsackievirus A16-related HFMS typically occur in the summer and autumn months. This infection most commonly affects those <5 years of age and the illness features a short fever prodrome followed by development of 4-8 mm ulcers on the tongue, buccal mucosa or gums. Following the enanthem, a vesicular eruption is usually seen over the hands more than the feet. Occasionally buttock lesions are noted, though non-tender. The right eye was injected with clear drainage and minimal crusting. Over the course of the next two days, he developed swelling and erythema of the eye lids and had a slight decrease in the ability to completely open the eye. History reveals that he lives on a farm and has multiple pet exposures, including cats, dogs and a chinchilla. He denies foreign body sensation or eye injury. On exam his extraocular muscles are intact and lymph nodes are palpated in front of the ear and along the cervical chain. Mild periorbital swelling and erythema are noted, although non-tender. The right conjunctiva is injected with noted white papules.

**Coxsackievirus A6 (CAV A6) HFMS:** Between Nov. 7, 2011, and Feb. 29, 2012, the CDC compiled 63 reports of HFMS where patients were described as having more severe and atypical rash.1 While most were <2 years of age, approximately 25 percent of cases were reported in adults, many of whom had contact with a child in child care. Rash and fever were more frequent and 20 percent were hospitalized—most for dehydration and severely painful lesions. The lesions in general were described as more widespread with rash on the face in 40 percent. In 4 percent of patients, shedding of nails was reported during the convalescent phase. The CDC was able to obtain specimens from lesions in about half of the cases. CAV A6 was detected by PCR or gene sequencing in 25 cases (74 percent). The report notes that CAV A6 was previously identified in international reports of outbreaks and that the United States strain was closely related. They were unable to confirm any epidemiologic information, however, to confirm the cases were related to importation.

One prior report from Taiwan described the skin lesions in their cases as being widespread with typical enanthem-exanthem plus perioral involvement in 22 percent, trunk or neck in 30 percent and generalized rash in 5 percent. More than half of the patients had peripheral desquamation and 37 percent nail abnormalities including Beau’s lines and nail separation (onychomadesis).

*References*


**Visual Diagnosis**

**WHAT’S THE DIAGNOSIS?**

A 15-year-old male presents with a four-day history of right eye erythema and fever to 38.7. Two days ago he noted that his eye was injected with clear drainage and minimal crusting. Over the course of the next two days, he developed swelling and erythema of the eye lids and had a slight decrease in the ability to completely open the eye. History reveals that he lives on a farm and has multiple pet exposures, including cats, dogs and a chinchilla. He denies foreign body sensation or eye injury. On exam his extraocular muscles are intact and lymph nodes are palpated in front of the ear and along the cervical chain. Mild periorbital swelling and erythema are noted, although non-tender. The right conjunctiva is injected with noted white papules.

**Which of the following is the most likely diagnosis in this patient?**

A. Bacterial conjunctivitis
B. Oculoglandular syndrome
C. Orbital cellulitis
D. Preseptal cellulitis
E. Viral conjunctivitis
Kathy Olson from the Lawrence Health Department called me recently regarding making the diagnosis of chickenpox in an immunized child (i.e. “breakthrough varicella”). While prior studies with Drs. Anne Gershon, Gene Shapiro and Marietta Vazquez project that only about 2 percent of kids who had two doses of vaccine are at risk for varicella, there is still a slight risk. Identifying children with varicella is important. While children with breakthrough varicella are less contagious than those who are not immunized, there is still a risk of transmission that could lead to outbreaks, particularly in under-immunized communities. Transmission to a household contact who is immunocompromised would be an additional concern.

The clinical manifestations of breakthrough varicella can be atypical (see photo). Children tend to have fewer lesions (50 verses 250), are less likely to have crops of lesions and the appearance of lesions is not the characteristic papules-turned-vesicles that crust that practitioners of lesions is not the characteristic papules-turned-vesicles that crust that practitioners tend to look for to make the diagnosis. More often, the lesions take on the appearance of “bug bites.” While serology would be diagnostic, this requires paired sera be available. It has also been noted that the routinely available serology are not sufficiently sensitive to detect vaccine-induced antibody. Dr. Gershon, Professor of Pediatrics at Columbia University in New York, is generally considered the go-to authority on questions related to the epidemiology, diagnosis, immunology, latency, prevention, and treatment of varicella and zoster virus infections. Her research was considered crucial to the licensure of the varicella vaccine in 1995 and her laboratory continues to offer FAMA testing (considered a research-only test) that can be used. This fluorescent antibody to membrane antigen methodology detects VZV-specific antibodies, and is sufficiently sensitive to detect vaccine induced immunity. Obtaining specimens for PCR is likely the best way to confirm the diagnosis as VZV does not grow well on culture. One could perform PCR on skin lesions (fluid or scabs) or, perhaps better, testing saliva for VZV DNA can successfully confirm the diagnosis.

While children with breakthrough varicella are less contagious than those who are not immunized, there is still a risk of transmission that could lead to outbreaks, particularly in under-immunized communities.

AAP UPDATES
THE EVER-GROWING IMPORTANCE OF IMMUNIZATIONS
Tom Tryon, MD, FAAP | District VI Representative, AAP Committee on Membership
Chief, Section of Urgent Care | Associate Professor, UMKC School of Medicine

From April 21-28, the nation recognized National Infant Immunization Week. This is also World Immunization Week, where health care communities across the globe unite to spread immunization campaign messages. Supported by the American Academy of Pediatrics, this initiative is a call to action against 14 vaccine-preventable diseases. Yet, with the successes of vaccines in our lifetime, we still face frequent and frustrating vaccine hesitancy avoidance and refusal from our families. In the most recent issue of the Missouri AAP Chapter newsletter, PedsLines, there is an excellent article “Responding with Empathy to Parents’ Fears of Vaccinations,” written by Dr. Ken Haller and Anthony Scalzo, both physicians in the St. Louis area.

The article begins with a patient vignette of a 3-month-old girl admitted to the hospital with pertussis. She spent five days in the hospital, eventually making a full recovery. The article is an excellent treatise looking at historical reasons responsible for parental distrust and nervousness regarding vaccinating their children. In the case of the 3-month-old, unvaccinated because of this parental nervousness and poor advice by the family’s chiropractor, the mother’s parting comment as she left the hospital was that she never wanted any family to have to suffer what they had gone through. She wanted her story to be used to “help convince other parents to vaccinate their kids on time.”

The article also points out the rise in vaccine-preventable cases in Missouri of pertussis and measles. These numbers reflect what is also being seen in other bordering states and in the nation. Most recently, Kansas had an outbreak of six cases of measles this past January in Garden City involving three members of two distinct families. The index cases were two family members who had traveled internationally. According to the KAAP website, “If an infant is exposed, the baby would need to be kept home and quarantined for 21 days. This means the parent(s) could miss 21 days of work which could be a financial burden to some families.” The article goes on to report that all non-immunized hospital staff who were exposed were also required to miss 21 days of work and that the Finney County Health Department had five full-time staff members who spent 90 percent of their time during the measles outbreak making daily house calls and only working on the measles cases.

Currently, the AAP is a partner in three worldwide initiatives, ONE, Shot@Life and Million Moms Challenge. Further, the current AAP President, Dr. Bob Block, highlighted these efforts in his “Letter from the President” in the latest edition of AAP News. That same issue has a front-page commentary from David Kimberlin titled, “If not vaccination, then what?” Dr. Kimberlin, who is the associate editor of the AAP Red Book and president-elect of the Pediatric Infectious Diseases Society, answers the question by articulating dangers from vaccine-preventable morbidity and mortality. He closes his article with the statement, “Vaccines are the lifeboats that God has sent to us. Please get in.” You are to be commended for the daily work you do encouraging patients to get in the lifeboat. It is making a difference, one child at a time.

References
4. www2.aap.org/immunization/about/ni.html
5. AAP News, Volume 33, Number 4, April 2012, p.6
Studies have shown that providers’ clinical estimate of the serum bilirubin level is unreliable. This is reflected in the 2009 AAP clinical practice guideline for the management of hyperbilirubinemia, which includes a clinical risk stratification and a recommendation that all newborns have bilirubin testing prior to nursery discharge by obtaining either a total serum bilirubin (TSB) or transcutaneous (TcB) level.2-4

Technology for TcB measurement has been available for more than 30 years, but debate continues to focus on the issue of reliability, especially in the outpatient setting. In 2005, Engle et al studied 121 jaundice infants at hospital follow up and using a TcB cutoff level of 13mg/dL, found a sensitivity of 1.0 to predict a TSB level <17mg/dL, suggesting TcB can predict relatively high TSB measurements, but concluding TcB is not a substitute for TSB.3 Maisels et al in 2009, studying a similar population, concluded that TcB can be a reliable screening method, concluding that a TcB cutoff of 14mg/dL predicted TSB levels of <17mg/dL.4 More recently, in a 2011 publication in Clinical Pediatrics, Wickremasinghe et al concluded that when using a cutoff of 13mg/dL, one did not accurately identify all babies with risk for significant hyperbilirubinemia (>75 percent on the Bhutani nomogram).5

Bosshart et al in the April issue of Pediatrics, investigated the reliability of a newer transcutaneous bilirubinometer that measures both TcB and blood volume fraction (BVF) of the skin. Finding that BVF is <1 percent of the traditional TcB measurements, the authors conclude that TSB and TcB are different physiological parameters. Their results found the new monitor was no better than other transcutaneous monitors and suggested that newer technology is still needed to replace measurement of TSB.6

For now, current technology does not allow transcutaneous monitors to replace TSB measurements. If transcutaneous measurement of bilirubin is performed, continue to obtain serum levels per the AAP recommendations: if TcB is at 70 percent of TSB level recommended for phototherapy, if TcB is greater than 75 percent on the Bhutani nomogram or if the TcB is >13mg/dL in the outpatient setting.

References
A 15-year-old male presents with a four-day history of right eye erythema and fever to 38.7. Two days ago he noted that his eye was injected with clear drainage and minimal crusting. Over the course of the next two days, he developed swelling and erythema of the eye lids and had a slight decrease in the ability to completely open the eye. History reveals that he lives on a farm and has multiple pet exposures, including cats, dogs, and a chinchilla. He denies foreign body sensation or eye injury. On exam his extraocular muscles are intact and lymph nodes are palpated in front of the ear and along the cervical chain. Mild periorbital swelling and erythema are noted, although non-tender. The right conjunctiva is injected with noted white papules.

Which of the following is the most likely diagnosis in this patient?

A. Bacterial conjunctivitis  
B. Oculoglandular syndrome  
C. Orbital cellulitis  
D. Preseptal cellulitis  
E. Viral conjunctivitis

Preferred Response: B - Oculoglandular syndrome

The patient in this scenario has Parinaud’s oculoglandular syndrome, which is characterized by one or more papular lesions in the conjunctiva (granulomatous conjunctivitis) and preauricular adenopathy. Systemic signs, such as low-grade fever, malaise and anorexia may be present as well. In this setting, the site of inoculation is the eyelid or conjunctiva. The most common cause of Parinaud’s oculoglandular syndrome is cat scratch disease (Bartonella henselae). Rare causes include: tularemia, HSV, EBV, and coccidiomycosis.

Cat scratch disease (CSD) most commonly presents with regional lymphadenitis (84 percent in one study) in the lymphatic drainage area adjacent to the initial scratch, with or without a papule at the site of the scratch. Typical lymph node sites of infection include: cervical (33 percent), axillary (27 percent) and inguinal (18 percent). Based on clinical presentation, 21 percent of cases in one review of cat scratch infection were described as atypical, including 7.4 percent of which were confirmed as Parinaud’s oculoglandular syndrome. Diagnosis is generally made clinically, but serologic testing can be diagnostic. If a negative initial serologic test for Bartonella is encountered, convalescent serology should be obtained approximately four weeks later.

Both viral and bacterial conjunctivitis are unlikely given that the child has no current or preceding upper respiratory tract symptomatology. Additionally, he does not have purulent discharge or significant crusting of the eyelids. Both preseptal and orbital cellulitis are initial considerations in this setting due to fever, swelling and erythema of the tissues surrounding the globe. However, papular conjunctivitis is not a feature of these infections and on exam the erythema is mild and no tenderness is noted. In addition, the ability to open his eye is only slightly decreased despite several days of symptoms. Finally, in the setting of orbital cellulitis, extracural movements are generally limited.

References
HPV is one of two cancer-causing pathogens for which a vaccine can prevent the cancers, hepatitis B being the other. But, uptake of HPV vaccine is low. Adolescents and their parents seem completely unmotivated to seek the vaccine. This may be because most adolescents and young adults live in the present, only occasionally considering future health issues. Yet clinicians who provide health care for these populations, are charged with providing preventive interventions.

The most recently reported data from the CDC on HPV-caused cancer is from 2004–2008 (See Figures 1 and 2) and gives us a frame of reference for counseling teens and parents about the potential benefits of HPV vaccines.

These data show that the average number of HPV-associated cancers among females was approximately 21,000 each year. This makes it more common than ovarian cancer and about equal to melanoma. In males, the rate was approximately 12,000 cases a year, nearly the same as brain cancer.

As many as 75 percent in both genders could be prevented by the currently available HPV vaccine. Both the bivalent and quadrivalent options protect against HPV 16 and 18, which are the two types of HPV that cause most cervical and anogenital cancers plus a proportion of oropharyngeal cancers.

While both vaccines prevent cervical precancers, the quadrivalent vaccine (contains types 6 and 11 in addition to 16 and 18) also prevents vaginal, vulvar and anal precancers.

So, nationally, approximately 32,000 cancers per year are caused by HPV and at least 20,000 are vaccine preventable. That translates to approximately 400 preventable cases in Missouri each year and somewhat fewer in Kansas.

This brings the importance of each clinician’s efforts into focus, even if the full benefits of HPV vaccine may not be readily apparent for your patients until they leave your care.

It’s relatively easy to remember to approach young adolescent females about whichever HPV vaccine your practice uses and young adolescent males about quadrivalent HPV vaccine. But, don’t forget that catch-up HPV vaccine is needed for females through age 26 years and for males through age 21 years.

Despite our efforts, only 32 percent of 13- to 17-year-old females had received three doses of HPV vaccine. The numbers of males was even fewer. So, when those older teens come for their college physicals or the occasional other visit, remember HPV vaccine in addition to the Tdap and meningococcal conjugate vaccine.

References
INFECTIOUS DISEASES FACULTY MEMBERS RECEIVE NATIONAL RECOGNITION

Angela Myers, MD, has been selected to the American Academy of Pediatrics PREP:ID Editorial Board, which is responsible for developing the content for a peer-reviewed, state-of-the-art online self-assessment program designed for pediatric infectious disease specialists. Barbara Pahud, MD, was selected to be one of the first members of the Pediatric Academic Society (PAS) Young Investigator Program, a national program that matches young researchers with a senior investigator/coach in their specific area of research.

ULTRASOUND SERVICES PROVIDED AT CHILDREN’S MERCY NORTHLAND

Children’s Mercy Hospitals and Clinics now offers ultrasound services at Children’s Mercy Northland for our clinic patients and on a scheduled outpatient basis. The service is available 8 a.m. to 4:30 p.m., Monday-Friday. You may order ultrasound service at Children’s Mercy Northland through the hospital’s centralized scheduling system at (816) 234-3272.

45TH ANNUAL CLINICAL ADVANCES IN PEDIATRICS SYMPOSIUM SET FOR NOV. 13-16

The 45th Annual Clinical Advances in Pediatrics Symposium (CAPS) at Children’s Mercy is Nov. 13-16. Visit www.childrensmercy.org/caps for more details about the event. Nationally recognized guest faculty scheduled to attend include:

Carol J. Baker, MD, Pediatric Infectious Diseases, Baylor College of Medicine, Houston
Barbara J. Howard, MD, Developmental and Behavioral Health, The Johns Hopkins University School of Medicine, Baltimore
John M. Kelso, MD, Allergy, Asthma and Immunology, University of California, San Diego School of Medicine, San Diego

DR. MARY ANNE JACKSON WINS ‘TAKE WING’ AWARD

Mary Anne Jackson, MD, Section Chief-Infectious Diseases, has been named winner of the Take Wing Award, an honor given to a graduate of the UMKC School of Medicine who has achieved excellence in their chosen field and surpassed the expectations in the practice of medicine, academics and/or research. The winner of this prestigious award provides the annual E. Grey Dimond Take Wing Lecture, as well as speaking at commencement ceremonies of the graduating class.

DR. JOHN LANTOS RECEIVES PELLEGRINO MEDAL

John Lantos, MD, Director of the Children’s Mercy Bioethics Center, was honored for his contributions to health care ethics during the 11th annual Healthcare Ethics and Law Institute (HEAL) conference sponsored by the Samford University (Birmingham, Ala.) McWhorter School of Pharmacy on April 13. Dr. Lantos received a Pellegrino Medal, which HEAL presents to world-renowned clinical ethicists.

CONTACT INFORMATION

The Link is produced monthly by Communications and Marketing with editorial guidance from the Associate Chair, Community and Regional Physician Collaborations.

For more information, contact:
Megan Stock
(816) 701-4073

The Link is available in print and e-mail newsletter formats. You may designate your preference (print, e-mail, both, neither) by going to www.childrensmercy.org/thelinkoptions.