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# Infectious Disease [ALERT]

Incisive Commentary and Clinical Abstracts on Current Issues in Infectious Diseases

ABSTRACT & COMMENTARY

# Seizures, Encephalopathy, and Vaccines — Evidence Fails to Support a Link

***By Hal B. Jenson, MD, FAAP***

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**Dr. Jenson reports no financial relationships relevant to this field of study.**

SYNOPSIS: A comprehensive, independent review of 10 years of all cases in the United States of seizures and encephalopathy reported as linked to vaccination showed that approximately one-quarter of cases had evidence of a pre-existing neurologic abnormality. Among those who developed chronic epilepsy, many had clinical features suggesting genetically determined epilepsy, especially Dravet syndrome.

SOURCE: Lateef TM, Johann-Liang R, Kaulas H, et al. Seizures, encephalopathy, and vaccines: Experience in the National Vaccine Injury Compensation Program. *J Pediatr* [In press] (published online ahead of print).

The National Childhood Vaccine Injury Act of 1986 requires physicians and others who administer vaccines to report occurrences of certain adverse events to the U.S. Department of Health and Human Services. The National Vaccine Injury Compensation Program (VCIP) receives claims and medical records of children with epileptic disorders following vaccination, documenting initial presentation, clinical course, vaccination history, developmental status, and clinical and laboratory evaluations.

Deidentified records were retrospectively reviewed of young children diagnosed with epilepsy, encephalopathy, or both after immunization and whose caretakers had petitioned the VCIP for compensation during the decade 1995 through 2005. Among a total of 222 claims submitted with "seizures" and/or "encephalopathy" as the alleged injury among children 2 years of age and younger, 165 had records with sufficient information to permit a comprehensive, independent review. The implicated vaccines included one or

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more administrations of whole-cell diphtheria-tetanus-pertussis (61%), acellular diphtheria-tetanus-pertussis (19%), mumps-measles-rubella (18%), *Haemophilus influenzae* type B (9%), and others (17%). Approximately 16% of children received more than one vaccine around the time of the alleged injury. The majority (59%) of claims listed seizures, 5% listed encephalopathy, and 36% listed seizures and encephalopathy as the alleged injury resulting from vaccination. More than half of cases were reported before six months of age, with three-quarters before 1 year of age; 45% had onset of seizures within 72 hours after vaccination; and 45% had documented fever.

Clinical cases were assessed independently by a single pediatric neurologist who developed a final study diagnosis on the basis of history, laboratory studies, imaging studies, EEG, and course of illness. The diagnoses included: 55% with epilepsy, including 18% of children having myoclonic epilepsy, almost all of whom were diagnosed with severe myoclonic epilepsy of infancy (SMEI), or Dravet syndrome; 7% with infantile spasms; 8% with febrile seizures; 18% with a specific diagnosis such as tuberous sclerosis; and 2% normal. Among the cases, before vaccination, 15% had pre-existing seizures, 10% had abnormal findings on neurological examination, and 4% were considered developmentally suspect.

## ■ COMMENTARY

Assessment of a causal relationship between vaccines and neurologic abnormalities in infancy is highly problematic because numerous rare neurologic disorders present during this age. Previous studies of the possible association between pertussis vaccination and neurologic disorders were performed prior to the recognition of SMEI, or Dravet syndrome, and before genetic testing was generally available. Many children previously diagnosed as having "pertussis encephalopathy" have been diagnosed as having SMEI, which is characterized clinically by febrile and afebrile, generalized and focal, clonic or tonic-clonic seizures presenting in the first year of life in an otherwise healthy infant. Many of these children have been shown to have a de novo mutation in the sodium channel gene SCN1A. In this retrospective analysis, although most cases occurred in infants and therefore were not easy to assess, approximately one-quarter of cases had evidence of a pre-existing abnormality of neurologic status.

Association does not prove causality. Because many genetic and underlying developmental abnormalities emerge during childhood, temporal association with vaccinations, most of which are administered during childhood, is likely. It has been difficult to demonstrate causality, or the lack of causality. The Institute of Medicine in 1994 stated that the evidence supporting a causal link of whole-cell pertussis vaccine and brain injury was "weak but not consistent." There are no epidemiologic studies to date that support a causal relationship of acellular pertussis vaccine and permanent neurological injury.

The results of this new analysis do not support concerns about vaccine safety, including use of the term "pertussis encephalopathy," which has been a diagnostic wastebasket for seizures of unknown etiology that begin in childhood. Physicians need to be circumspect about using this term as a clinical diagnosis and also careful suggesting to families that vaccinations are a cause of seizures and encephalopathy. ■

ABSTRACT & COMMENTARY

# Fusobacterium as a Cause of Pharyngitis in Young Adults

***By Dean L. Winslow, MD, FACP, FIDSA***

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**Dr. Winslow reports no financial relationships relevant to this field of study.**

SYNOPSIS: Three hundred twelve students presenting to a university student health clinic with sore throat and 180 asymptomatic students had throat swabs taken and the samples were tested by PCR for *Fusobacterium necrophorum*, *Mycoplasma pneumonia*, group A streptococci, and group C/G streptococci. *Fusobacterium necrophorum*-positive pharyngitis occurs more frequently than group A streptococcal pharyngitis in this population and clinically resembles streptococcal pharyngitis.

SOURCE: Centor RM, et al. The clinical presentation of Fusobacterium-positive and streptococcal-positive pharyngitis in a university health clinic — a cross-sectional study. *Ann Intern Med* 2015;162:241-247.

Three hundred twelve university students (aged 15-30) presenting to a student health clinic with acute sore throat and 180 asymptomatic students were sampled by throat swab and the specimens were analyzed using PCR for *F. necrophorum*, *Mycoplasma pneumonia*, group A streptococci (GAS), and group C/G streptococci (GCS/GGS). *F. necrophorum* was detected in 20.5% of patients and 9.4% of controls. GAS was found in 10.3% of patients and 1.1% of asymptomatic students. Group C/G streptococci were detected in 9% of patients and 3.9% of controls. *Mycoplasma pneumonia* was found in 1.9% of patients and 0 controls. Clinical features of *F. necrophorum*-positive and GAS/GCS/GGS-positive cases were similar as assessed using the Centor score (fever, lack of cough, swollen, tender anterior cervical lymphadenopathy, and tonsillar exudates).

## ■ COMMENTARY

This is an interesting study that uses modern molecular techniques to understand the etiology of pharyngitis in young adults. While both Fusobacterium and Beta hemolytic streptococci are commonly associated with asymptomatic carriage in young adults, it is clear that both of these organisms are significant pathogens. (Lemierre's syndrome is associated with *F. necrophorum* and various suppurative complications are associated with streptococci, although paradoxically Lemierre's syndrome rarely follows clinical tonsillitis.)

Some important take-home points that can be gleaned from this paper include that penicillin is probably the antibiotic of choice in treating adolescent and young adult patients with high Centor scores, especially tonsillitis. All Fusobacteria are resistant to macrolides, and macrolide resistance is now common in GAS. Fortunately, these organisms remain susceptible to penicillin. It should be remembered that the results presented in this paper should not be extrapolated to pre-adolescent patients in whom both Fusobacterium and GCS/GGS are distinctly uncommon. While it is true that *F. necrophorum* may not uncommonly be associated with asymptomatic pharyngeal colonization, its pathogenicity is significant and testing (and treating) for this organism in patients in whom the pre-test probability of its pathogenicity is high, should be considered. Testing for *F. necrophorum* may become more practical and cost-effective as low cost multiplex assays are developed. ■

ABSTRACT & COMMENTARY

# Acute Leukemia Patients Still Plagued by Vancomycin-Resistant Enterococci

***By Joseph F. John, Jr., MD***

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**Dr. John reports no financial relationships relevant to this field of study.**

SYNOPSIS: Fifteen (7%) of 214 patients hospitalized with newly diagnosed acute leukemia developed bacteremia due to vancomycin-resistant enterococci; 12 (80%) of the 15 had stool colonization with the organism.

SOURCE: Ford CD, Leopansir BK, Haydoura S, et al. Frequency, risk factors and outcomes of vancomycin-resistant Enterococcus colonization and infection in patients with newly diagnosed acute leukemia: Different patterns in patients with acute myelogenous and acute lymphoblastic leukemia. *Infect Control Hosp Epidemiol* 2015;36:47-53.

The enterococcus is ever with us, a commensal and a low-level pathogen, except for its ability to cause morbidity and occasionally mortality in bloodstream infections. Vancomycin-resistant enterococci (VRE), primarily species specific *Enterococcus faecium*, emerged 20 years ago, and VRE still poses a threat. During the past two decades, VRE has been the subject of widespread publication, with the latest flurry of publications coming between 2007and 2012. Many of the risk factors have been determined in various settings, but a proven strategy for prevention has not been devised.

From the LDS Hospital in Salt Lake now comes a study by Ford et al of VRE bloodstream infections in patients with newly diagnosed acute leukemia. They studied 214 consecutive patients with acute leukemia for colonization and related bloodstream infections with VRE. The study covered the years 2006 to 2014. Patients during the time of their leukemia were housed in a laminar-flow room in a ward dedicated to patients with hematologic malignancies. All patients had central catheters and all patients had weekly stool cultures for VRE. One hundred seventy of the patients had AML. The mean hospital admission lasted 29 days, with a range of 1-69 days.

Fifteen (7%) of the patients acquired a bloodstream infection with VRE. Only 3% had stool colonization with VRE on admission, and 35% acquired VRE after admission. Almost 10% developed toxin-positive stool for *C. difficile* and 80% of the patients with bloodstream infection had VRE stool colonization. Variables associated with stool colonization by both univariate and multivariate analysis included exposure to corticosteroids and carbapenems, and an increased number of stools per day. When antimicrobials were analyzed separately, only carbapenems were a significant risk factor (P = 0.002).

The molecular analysis done by repetitive element PCR was very interesting considering the patients were all housed on the same ward over many years. Of 24 strains analyzed, 21 had highly similar or identical patterns (my reading) with 80% genetic similarity. Two of the three remaining had about 10% less genetic similarity, leaving one isolate with a highly divergent type. The authors report nine of the isolates as an identical molecular group. Of nine bloodstream infection/stool pairs, 78% had identical pattern types. Hospital costs were doubled in patients with bloodstream infections due to VRE, primarily due to prolonged length of stay (LOS).

## ■ COMMENTARY

What have we learned about VRE in 20 years? We know that prolonged hospitalization, hematologic malignancies, neutropenia, exposure to antibiotics, stool colonization, length of stay, and probably central lines are risk factors for VRE bloodstream infection. Even though the numbers are small, this current study adds evidence that most bloodstream infections are related to prioir colonization with VRE. There is a constant "colonization pressure" on units such as the one in this study. We also know the intestinal microbiome is a very complex entity, with hundreds of species of bacteria colonizing the normal gut. Yet we do not know which microbiomes are more protective than others from high-grade VRE colonization. If we can solve that problem, perhaps using probiotics, find nonpathogenic strains of VRE or vancomycin-susceptible enterococci to colonize the at-risk gut, or invent a useful immunization strategy, we can reduce the gastrointestinal colonization that is linked to bloodstream infection.[1]

Additionally, there may be new strategies based on altering the microbial burden in the environments of high-risk wards. Perhaps the use of sterilizing tough surfaces like those containing a high percentage of copper, periodic disinfection of the environment with UV light or hydrogen peroxide, or newer forms of surface decontamination will lessen the risk of GI colonization with VRE.

The authors also are concerned with the persistence of similar strains during the six years of the study. Is there a way to rid a unit like this of the predominating strains of VRE? Some of the strategies described above may be used in conjunction with newer infection control methods of preventing transmission and colonization, such as very early detection of colonization using PCR or protein-based rapid diagnosis.

For now, the outlook is not good for those patients who do become colonized with VRE. Their risk of bloodstream infection after colonization increases steadily with exposure to steroids, broad-spectrum antibiotics, and length of stay. Survival itself in a VRE group compared to controls is reduced by 20% at 12 months into their leukemia. Clearly there is a lot more work to be done to understand how best to protect these very vulnerable patients from infection with VRE. ■

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ABSTRACT & COMMENTARY

# Steroids for Severe Community-Acquired Pneumonia: More Evidence or More Uncertainty?

*By Richard R. Watkins, MD, MS, FACP*

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**Dr. Watkins has received research support from Forest Laboratories.**

SYNOPSIS: A multicenter, randomized, double-blind, placebo-controlled trial involving patients with severe community-acquired pneumonia and evidence of high inflammation found less treatment failure in those who received steroids. However, in-hospital mortality did not differ between the groups.

SOURCE: Torres A, et al. Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response. *JAMA* 2015;313:677-686.

Community-acquired pneumonia (CAP) is the leading cause of mortality from infection in industrialized countries, and treatment failure occurs in 10-20% of cases despite appropriate antibiotic therapy. Thus, effective treatment strategies that reduce the burden of CAP would have a major impact on public health. Several previous studies that investigated the role of corticosteroids in CAP produced mixed results. Torres and colleagues hypothesized that corticosteroids modulate the immune response in severe CAP, thereby decreasing treatment failure.

The study was conduced at three teaching hospitals in Spain. Patients were prospectively enrolled between June 2004 and February 2012. The inclusion criteria included age > 18 years, had symptoms of CAP, a new infiltrate on chest radiograph, met severe CAP criteria, and had a C-reactive protein (CRP) greater than 150 mg/L on admission. Patients were excluded if they had previously been on corticosteroids, had HIV, had uncontrolled diabetes mellitus, had gastrointestinal bleeding in the preceding 3 months, or had influenza or a condition that required treatment with methylprednisolone. All enrollees were randomized to receive either intravenous methylprednisolone or placebo for five days started within 36 hours of hospital admission. The primary endpoint was the rate of treatment failure, which the authors divided into early (clinical deterioration within 72 hours of treatment) and late (defined as radiographic progression, persistence of respiratory failure including mechanical ventilation, development of shock, and death between 72 hours and 120 hours after treatment initiation). Secondary endpoints were time to clinical stability, length of stay, and in-hospital mortality. CRP levels were obtained on days 1, 3, and 7 of treatment.

A total of 120 patients were randomized, 61 to the methylprednisolone group and 59 to the placebo group. Ninety patients (75%) were admitted to the intensive care unit. The antibiotic regimens chosen, mostly ceftriaxone with levofloxacin or azithromycin, did not differ between the groups. There was significantly less treatment failure in the steroid group (8 patients [13%]) compared to the placebo group (18 patients [31%] (P = 0.02). There were no statistically significant differences in the secondary endpoints between the steroid and placebo groups. At hospital day 3, decreases in CRP levels were greater in the steroid group, while those patients with persistent high CRP at day 7 had a higher percentage of treatment failure and mortality.

## ■ COMMENTARY

This study showed that patients with severe CAP who received methylprednisolone had reduced inflammation and less treatment failure compared to those who received placebo. However, these results need to be interpreted with caution. First of all, baseline cortisol levels were not measured. It is possible that undiagnosed adrenal insufficiency may have led to more treatment failures, especially in critically ill patients admitted to the ICU. Second, the placebo group had a higher proportion of patients with septic shock and acute respiratory failure requiring mechanical ventilation. This could be interpreted that steroids were given to patients who were less ill and therefore expected to have better outcomes. Third, the main treatment difference between the two groups was mainly

due to less radiologic progression 72 hours or more from time of randomization. As noted in an accompanying editorial, the two likely explanations for this phenomenon are worsening pneumonia and the development of acute respiratory distress syndrome (ARDS).[1] It seems illogical that steroids would help with the former condition but plausible they might modulate the latter. One theory is that ARDS is caused by cytokine release from a Jarisch-Herxheimer-like reaction in tissue with a high bacterial genomic load after the initiation of antibiotics. Thus, steroids may block this inflammatory reaction from occurring. But additional larger and more definitive studies are necessary to confirm that less radiologic progression leads to improved mortality.

In the current (albeit outdated) IDSA/ATS clinical practice guidelines for CAP,[2] CRP is not a recommended diagnostic test, although it is used in European countries.[3] Torres and colleagues used a CRP level of 150 mg/L or greater as an inclusion criterion for quantifying inflammation, yet only 57% of eligible patients (162/284) had this level. Therefore, the patients in their study represented only a fraction of those with severe CAP. The possible benefits of steroids for patients with severe CAP and lower CRP levels remain to be elucidated.

Because the immunosuppressive effects of steroids could theoretically worsen an already severe infection, it is important to recall the old adage "primum non nocere" (first, do no harm). The results of the study by Torres and colleagues need further confirmation before the widespread use of steroids in severe CAP can be endorsed. ■

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ABSTRACT & COMMENTARY

# Preventing Active Tuberculosis in Children


***By Philip R. Fischer, MD, DTM&H, and Shemonti R. Hasan***

*Dr. Fischer is Professor of Pediatrics, Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN. Ms. Hasan is a student at Mayo Medical School.*



**Dr. Fischer and Ms. Hasan report no financial relationships relevant to this field of study.**



SYNOPSIS: A three-month course of weekly rifapentine and isoniazid is safe and at least as effective as nine months of daily isoniazid in preventing tuberculosis in children aged 2 to 17 years.

SOURCE: Villarino ME, et al. Treatment for preventing tuberculosis in children and adolescents. *JAMA Pediatr* 2015;169:247-255.


In a randomized clinical trial, the effectiveness of 12 weekly directly observed doses of rifapentine and isoniazid was compared to the effectiveness of standard treatment (self-administration of daily isoniazid for nine months). Patients aged 2 to 17 years with latent tuberculosis at 29 sites in Brazil, Canada, Hong Kong, Spain, and the United States were enrolled from 2001 to 2010, with follow-up until 2013.

Nine hundred five children out of the 1058 total who enrolled were eligible for analyzing effectiveness. Of the 471 receiving the combination therapy, 415 (88.1%) completed treatment, while only 351 of 434 (80.9%) on isoniazid alone completed treatment (p = 0.003). Between the two treatment groups, discontinuation due to adverse events was similar and less than 1%. No one in the combination-therapy group developed tuberculosis, whereas three children (0.74%) developed the disease in the isoniazid-only group (p = 0.098).

Results from this clinical trial demonstrated that the combination therapy had a similar (non-inferior) effect in preventing latent tuberculosis infection compared to isoniazid-only therapy. However, the completion rate for the combination-therapy group was higher than the isoniazid-only group.

## ■ COMMENTARY

Tuberculosis continues to be a major problem worldwide, and children are at particular risk. Prevention of illness in TB-exposed and infected children is especially important since children are at

relatively increased risk of severe disease, are more likely to progress from latent infection to illness, and have more potential years of life at risk of TB illness. Fortunately, children also tolerate preventive TB treatment better than adults do. However, adherence to long treatment regimens is problematic for asymptomatic children, and simplified yet effective treatment courses would be helpful.

Recent investigation has suggested that shorter, simpler courses of preventive TB medications are safe and effective in healthy yet infected adults.[1] Aware of favorable pharmacokinetic data for the use of rifapentine in children, the investigative team undertook the current pediatric study and found similar results. This offers a helpful new option for the treatment of TB-exposed and TB-infected children.

However, there is already vast variation in the treatment of latent tuberculosis infection in children. For instance, national guidelines include either three months of rifampin and isoniazid or six months of isoniazid in the United Kingdom and South Africa, nine months of isoniazid in the United States, and six months of isoniazid per the World Health Organization.[2] Having more uniform, consistent recommendations might help improve compliance and adherence among patients between various sites.

Also, the current study was not only a comparison of various medication regimens. The short-course combined therapy subjects had directly observed therapy, and the longer isoniazid group had self-administered medication. Some of the variation in outcome might have been due to observation and contact with medical providers rather than simply due to medication differences. And, even the control single medication group had more careful follow-up than might be provided in regular clinical situations. A key to effectiveness of tuberculosis therapy is adherence, so "real world" treatments will have to be implemented carefully to ensure adequate delivery of medication.

As pointed out in an editorial accompanying Villarino's paper, young children are of particular concern for latent TB infection treatment, and the current paper did not include very many pre-schoolers.[3] Future studies of younger children will be useful as various treatment regimens and dosing schemes are evaluated.

Even while further research continues, the rigorous study by Villarino is very helpful. Clinicians now have a shorter, simpler regimen to consider in treating latent tuberculosis infection in children aged 2 to 17 years. ■

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# Reservoir Bugs: CRE in Long-term Acute Care Hospitals Threatens to Spread to Other Facilities

*Bundle using chlorhexidine cloths for patients cuts CRE rates*

***By Gary Evans***


*Gary Evans is executive editor of Hospital Infection Control and Prevention.*



**Gary Evans reports no financial relationships relevant to this field of study.**


With a combination of severely ill patients, high antibiotic use, and lengths of stay measured in weeks, long-term acute care (LTAC) hospitals have been described as a perfect storm for emergence of multidrug-resistant organisms (MDROs).

Among the panoply of MDROs is one of utmost concern, a group of bacteria that are resistant to virtually all available antibiotics: Carbapenem-resistant Enterobacteriaceae (CRE).

"CRE may be the most serious contemporary antibiotic resistance threat because of the number of different resistance mechanisms, concomitant resistance to all or nearly all alternative antibiotics, high attributable mortality associated with invasive

infection, and the ability of these pathogens to spread rapidly across geographic regions," the authors of a recently published study conclude.[1]

In that regard, the most widely dispersed type of CRE in the U.S. is carbapenem-resistant *Klebsiella pneumoniae* (KPC). In giving CRE its highest public health threat rating of "urgent," the Centers for Disease Control and Prevention emphasized that while some "4% of U.S. short-stay hospitals had at least one patient with a serious CRE infection during the first half of 2012 — about 18% of LTACs had one."[2]

Evidence continues to accumulate that the more than 400 LTACs nationally are at risk of becoming CRE reservoirs, as the emerging pathogen establishes an endemic presence that is hard to eradicate. To add historical inevitability to this toxic mix, communication breakdowns between long-term care facilities and hospitals about transferred residents or patients colonized or infected with MDROs has been a longstanding source of controversy. Regardless of whether the CRE originally came in through a hospital patient, the problem is that the care delivery model in LTACs can amplify the effect and serve as a reservoir for future transmission across the continuum.

"LTC facilities have long been documented as 'reservoirs' of MDR organisms," researchers report.[3] "LTACHs, where antibiotic use is considerable and patients often come from ICUs requiring mechanical ventilation and invasive devices, add a new and heightened dimension to this problem. Therefore, the dissemination of carbapenem-resistant organisms in these settings is worrisome."

Given the possibility of a practically pan-resistant pathogen moving across the health care continuum, the CDC recommends "When transferring a patient, require staff to notify the other facility about infections, including CRE. Participate in regional and facility-based prevention efforts designed to stop the transmission of these organisms."[4]

In the absence of such measures, CRE can spread throughout regional health systems, as happened in Chicago in 2008 when a cluster of KPC cases at one LTACH formed the epicenter of a regional outbreak that spread to 26 other health care facilities.[5] In the aftermath of that outbreak and with increasing prevalence of KPC colonization among patients in Chicago area LTACHs, a regional collaborative and research effort was launched. The latest example of that effort comes in a recently published paper,[1] which found that a bundle of infection control interventions that included chlorhexidine baths for patients sharply reduced the rate of colonization and infection in four LTACHs in Chicago with high endemic KPC prevalence.

The bundle intervention included:
- screening patients for KPC rectal colonization upon admission and every other week;
- contact isolation and geographic separation of KPC-positive patients in ward cohorts or single rooms;
- bathing all patients daily with 2% chlorhexidine gluconate (CHG)–impregnated cloths;
- health care worker education and adherence monitoring, with a focus on hand hygiene.

### KPC Colonization Drops

The study was conducted between February 1, 2010, and June 30, 2013, with 3,894 patients enrolled during the pre-intervention period (lasting from 16-29 months), and 2,951 patients were enrolled during the intervention period (lasting from 12-19 months).

Though KPC prevalence on admission remained high, the incidence rate of KPC colonization fell 50% during the intervention, going from 4 to 2 acquisitions per 100 patient-weeks. Compared to pre-intervention, average rates of clinical outcomes declined during intervention: KPC in any clinical culture (3.7 to 2.5/1000 patient-days); KPC bacteremia (0.9 to 0.4/1000 patient-days): all-cause bacteremia (11.2 to 7.6/1000 patient-days) and blood culture contamination (4.9 to 2.3/1000 patient-days).

### Chlorhexidine Bathing May Be Key Measure

The chlorhexidine bathing was probably the intervention most responsible for the sharp declines in all cause bloodstream infections and skin decolonization, the authors noted.

"We found for the individual patient it was reducing their risk of infection by significantly reducing their skin burden of organisms," says lead author **Mary K. Hayden**, MD, infectious disease physician at Rush University Medical. "But really the problem with a bundle is you can't say with any kind of certainty which component [had the most effect]."

In contrast, declines in KPC incidence and prevalence were more gradual, presumably reflecting the greater effort needed to control cross-colonization in a setting of high KPC rates on admission and ongoing colonization pressure.

In research that preceded the current study, Hayden and colleagues determined that skin colonization of patients was a much bigger factor than environmental contamination.[6]

"If we had found a lot of environmental contamination, then we would have included enhanced environmental cleaning in our bundle," she says. "I know that other studies have found environmental contamination, but we really found very little, so we did not include that in our bundle. But we found lots of KPC on patient skin — over 90% who were tested in the previous study had KPC on their skin. And over 50% of the skin sites tested were positive for KPC. So we did include chlorhexidine in the bundle."

Factors contributing to spread within the facility likely include the acuity of patients, high use of medical devices, and the "hands-on care" these patients require, she adds. "The patients admitted there typically have lots of health care exposure, medical device exposures, and lots of antibiotic exposure," she explains. "They have had prolonged or sometimes multiple prior hospital stays. So they are already set up for antibiotic resistance organisms. In our paper we found that 20% of patients on average who are admitted to the LTACHs are colonized with KPC at the time of admission."

Though hand hygiene was emphasized, compliance with infection control measures was not reported in the paper.

"New colonizations were detected in the facility from patients who presumably had acquired KPC from another patient," Hayden says. "We were able to reduce what we are assuming was cross transmission of KPC in the facility. The rate of new cases of colonizations declined steadily during the intervention, from about 4 cases per 100 patients at risk per week, down to about 2. It was about half by the end of the study."

Patient transfers have been "a huge part of the problem," she said, noting that another aspect of their ongoing research is to improve interfacility communication. "Awareness of the problem is really important in order to be able to control it and prevent spread if it enters your facility."

To address the problem, Illinois public health officials and clinicians developed the Extensively Drug Resistant Organism (XDRO) Registry, which is designed to improve inter-facility communication on patients who have tested positive for CRE. The registry stores CRE surveillance data and has features that can help facilities track their CRE submission history. Creation of the registry required the state public health department to amend the Control of Communicable Diseases Code, which now requires reporting of CRE to state public health.

CRE-positive cultures per patient stay must be reported to the XDRO registry within 7 calendar days after the test result is finalized. All hospitals, hospital-affiliated clinical laboratories, independent or free-standing laboratories, longer-term care facilities, and long-term acute care hospitals in Illinois are required to report CRE isolates.

### CRE Recommendations for Facilities, Clinicians

To meet the threat of CRE, here are some of the basic measures CDC recommends for health facilities and clinicians:
- Require and strictly enforce CDC guidance for CRE detection, prevention, tracking, and reporting.
- Make sure their lab can accurately identify CRE.
- Understand their prevalence in the facility and in the region.
- Identify colonized and infected patients in the facility and ensure precautions are implemented.
- When transferring a patient, require staff to notify the other facility about infections, including CRE.
- Participate in regional and facility-based efforts designed to stop the transmission of these organisms.
- Notify health departments of outbreaks.

Steps clinicians should take:
- Know if patients with CRE are hospitalized at your facility, and stay aware of CRE infection rates. Ask if a patient has received medical care somewhere else, including another country.
- Place patients currently or previously colonized or infected with CRE on Contact Precautions. Whenever possible, dedicate rooms, equipment, and staff to CRE patients.
- Wear a gown and gloves when caring for patients with CRE.
- Perform hand hygiene — use alcohol-based hand rub or wash hands with soap and water before and after contact with patient or their environment.
- Alert the receiving facility when you transfer a CRE patient, and find out when a patient with CRE transfers into your facility.
- Make sure labs immediately alert clinical and infection prevention staff when CRE are identified.
- Prescribe and use antibiotics wisely.
- Discontinue devices like urinary catheters as soon as no longer necessary.

**REFERENCE**

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"So in Illinois it is required that if you have a CRE case you record that information or you send that information electronically to this registry," Hayden says.

"Now whenever I get a patient in my facility and I am suspicious of them having CRE, I can ping the registry and it is all coded and HIPA compliant — I can find out if my patient has registered before at another facility. They're working towards automating that so that instead of the IP having to go manually into the registry, each time she gets a new [patient] it automatically sends the information."

It is hoped that improved communication and the use of bundles like the one described can reduce the presence of CRE in LTACHs and prevent transmission to downstream facilities. While labor intensive, the bundle could be an option for facilities that are having recurrent CRE problems. "We were very concerned about getting this problem under control as quickly as possible," Hayden says. "There needs to be more studies, but if you know your LTACH has a problem and you want to get on top of it, this is definitely a way that I would approach it based on our experience." ■

## REFERENCES


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Infectious Disease [ALERT]

# Updates

By Carol A. Kemper, MD, FACP

## Water Birth Death

Fristchel E, et al. Fatal legionellosis after water birth, Texas, USA, 2014. *Emerging Infectious Diseases* www.cdc.gov/eid. 2015;21(1):130-132.

Although statistics are few, home water births appear to be increasingly popular in the United States and the United Kingdom, and are making an appearance in Australia, France, and in other parts of the modern world. Celebrated in the 2003-2005 British television series "William and Mary," Mary, who was herself a certified midwife in the U.K., delivers Martin Clune's child — out of wedlock — and in a spa tub. Yet, concerns have been raised about the adequacy of the training for midwives and appropriate maintenance of equipment for home water deliveries.

This report documents the sad demise of a 6-day-old baby boy admitted to hospital in January 2014 with sepsis, respiratory failure, and loose stool in Texas. The infant immediately required extracorporeal membrane oxygenation. Initial cultures were negative for the usual organisms leading to post-partum sepsis, but astute critical care staff, knowing about the home water birth and suspecting something different, obtained tracheal aspirates and legionella urinary antigen, both of which were positive for *Legionella pneumophila* at day 4 of hospitalization. Despite aggressive measures, the infant died after 19 days of hospitalization. The nine-month pregnancy had been uncomplicated, and the infant had appeared to be a normal healthy baby boy.

Investigation by Texas state health authorities revealed several areas of concern. Well water was used to fill the home spa tub and, in preparation for the delivery, allowed to sit and circulate at approximately 37 degrees for two weeks prior to delivery. The water was exchanged two days prior to delivery. The water was treated with enzyme tablets but not chlorine. The tub was a recreational spa tub with internal piping and jets, rendering it difficult to sterilize. This type of tub is not licensed for use as medical equipment. The new mom was transferred to a regular bathtub following delivery, which was also filled with well water, and allowed to hold the infant.

Both well water and swabs of the tub failed to yield Legionella, although by the time the investigation was

proceeding, the spa tub had been cleaned, disinfected, and put in storage. No comment was made in this report whether the home hot water heater or tub was tested.

Cases of Legionella related to home water baths and whirlpools may occur, although cases in infants are rare. Further, inadequately chlorinated home water spas and hot tubs may be a source for Pseudomonas, non-tuberculous mycobacteria, and fungi. I remember well a regional outbreak of pedicure-associated non-tuberculous mycobacterial folliculitis. Although the source for the outbreak was not ever identified, the whirlpool chairs used to soak feet were dismantled by our public health officer for inspection. Despite previous "cleaning," the internal jets and piping were coated in slime, debris, and hair. I can just imagine what a spa tub used for home delivery might look like on the inside. Yikes.

This case led to more formal public health recommendations regarding the appropriate type and maintenance of equipment used for home deliveries, specific requirements for water treatment, as well as recommendations for education and training requirements for midwifery certification.

## Out, Damned Spore!

Landelle C, et al. Contamination of healthcare workers' hands with *Clostridium difficile* spores after caring for patients with *C difficile* infection. *Infection Control and Hosp Epidemiol* 2014;35(1):10-15.

Despite our best efforts as Infection Control staff, routine surveillance of all high-risk admission using PCR, strict isolation and contact precautions, private rooms, and amped up daily cleaning and terminal bleach cleaning of all *C. difficile* rooms, and a recent hand hygiene campaign, our hospital continues to experience a modest level of hospital-acquired *C. difficile* infection (CDI). While some of these cases were no doubt occult carriers on admission, and later developed symptoms of CDI in hospital, some patients likely acquired CD in the hospital — either from environmental contamination or from hands. Hands remain the most likely suspect.

Studies suggest that, even despite efforts to cleanse hands, both vegetative and spore forms of CD persist on hands of 14% to 59% of health care workers providing care to patients with CD. These spores may resist routine disinfection in the hospital and persist in the environment. These investigators developed a technique for destroying the vegetative forms of CD on hands, and recovering only the spores for a colony count determination.

Health care workers were observed at a 950-bed university hospital on six different wards (critical care, one surgical ward, and four medical wards) over a period of three months. Health care workers were divided into those who were providing care for a CDI patient and those who were not. Every contact was documented, and risk stratified by the duration of contact and the type of contact (high-risk activities were those involving exposure to feces such as bathing the perineum or diaper changes). A CD case was defined as a patient with diarrhea and a positive toxin test. All such patients were immediately placed in strict contact isolation in a private room until 48 hours after diarrhea had resolved. Infection control precautions included the use of gown and gloves on entry to rooms, alcohol gel before donning gloves, before any aseptic task, and hand washing with soap and water followed by alcohol gel after glove removal, as well as daily room cleaning with a hypochlorite solution.

Results of hand sampling for 66 "exposed" health care workers providing care to 7 CDI patients were compared with a control group of 44 unexposed health care workers, who provided care to 16 non-CDI patients. CD spores were recovered from 16/66 (24%) of the exposed group compared with none of the unexposed health care worker group. On average, two spores were found per positive hand (range, 1-6). For the exposed group, 30/386 (7.8%) of contacts with the patient and/or room were without gloves. Seven of the 16 health care workers with contaminated hands had at least one contact without gloves. This also means that 10.6% of health care workers failed to use gloves when caring for a CDI patient, despite every reason to do so.

In bivariate analysis, hand contamination was associated with high-risk activities, a longer duration of contact, a higher number of contacts, as well as contact without gloves.

Nursing assistants were more likely to have hand contamination (42%) than physicians (23%) or nurses (19%), consistent with the nature of their duties. Despite the fact that physicians had fewer high-risk contacts (only 4% of their exposures were considered high risk), they proportionately had a greater frequency of hand contamination. Logistic regression confirmed that two factors were highly correlated with hand contamination: high-risk activities and contact without gloves.

Infection preventionists know that, despite strict policies, signage, education, and ongoing surveillance, health care workers sometimes fail to don gloves when caring for a patient in isolation. This problem needs to be confronted in a more pecuniary way. ■

## CME INSTRUCTIONS

To earn credit for this activity, please follow these instructions:

1. Read and study the activity, using the provided references for further research.
2. Scan the QR code to the right, or log on to **AHCMedia.com** to take a post-test; tests can be taken after each issue. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice, or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the test, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly.

## CME QUESTIONS

**1. A reasonable treatment option for a 7-year-old with latent tuberculosis infection:**

A. is not available

B. must include nine months of oral therapy

C. could include three months of combined therapy

D. is not needed in developed countries

**2. Centor and colleagues identified targeted organisms by PCR of throat swabs of young adults with pharyngitis. Which of the following describes the correct frequency of identification in decreasing order of identifications?**

A. Group A streptococcus followed by Group C streptococcus followed by *Mycoplasma pneumoniae* followed by *Fusobacterium necrophorum*

B. *Fusobacterium necrophorum* followed by Group A streptococcus followed by Group C streptococcus followed by *Mycoplasma pneumoniae*

C. *Mycoplasma pneumoniae* followed by *Fusobacterium necrophorum* followed by Group A streptococcus followed by Group C streptococcus

D. *Fusobacterium necrophorum* followed by *Mycoplasma pneumoniae* followed by Group A streptococcus followed by Group C streptococcus

**3. Which of the following is correct with regard to the study by Ford and colleagues of vancomycin-resistant enterococci (VRE) in patients with acute leukemia?**

A. Thirty-five percent of patients had VRE stool colonization on admission, but this subsequently decreased to 3%.

B. Eighty percent of patients with VRE bacteremia had evidence of VRE stool colonization.

C. Among antibiotics, only cefepime was identified as an independent risk factor for VRE stool colonization.

D. Genetic typing found that stool and blood VRE isolates rarely matched.

## CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- discuss the diagnosis of infectious diseases;
- explain current data regarding the use of new antibiotics for commonly diagnosed diseases and new uses for traditional drugs;
- discuss the latest information regarding risks, benefits, and cost-effectiveness of new and traditional diagnostic tests; and
- discuss new information regarding how infectious diseases are transmitted and how such information can lead to the development of new therapies

## [IN FUTURE ISSUES]

U.S. Ebola response: Current status and lessons learned

Community-acquired pneumonia in children