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Infectious Disease [ALERT]

Incisive Commentary and Clinical Abstracts on Current Issues in Infectious Diseases

ABSTRACT & COMMENTARY

ART for Life's Sake: The Profound affect of Antiretroviral Therapy on HIV in Africa

Antiretroviral therapy could save 28 million life-years by 2030

By Dean L. Winslow, MD, FACP, FIDSA

Clinical Professor of Medicine and Pediatrics Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, Associate Editor of Infectious Disease Alert

Dr. Winslow is a consultant for Siemens Diagnostic.

SYNOPSIS: Modeling was used to estimate the survival benefits of antiretroviral therapy in patients in South Africa initiating antiretroviral therapy in 2004-2011. Survival benefits ranged from 9.3 to 10.2 life-years across 8 cohorts with a total population lifetime benefit of survival being 21.7 million life-years.

SOURCES: April MD, et al. The survival benefits of antiretroviral therapy in South Africa. *J Infect Dis* 2013;(published online Dec 34): 1-9.

Survival benefits in adults attributable to antiretroviral therapy (ART) initiated in South Africa since 2004 were quantified using the Cost-Effectiveness of Preventing AIDS Complications-International model (CEPAC) simulating 8 cohorts of HIV-infected patients initiating therapy each year 2004-2011. Model inputs included cohort-specific CD4+ count at ART initiation, 24 week ART suppressive efficacy (78%), limited second-line ART availability, 36 month retention in care (55%-71%). Lifetime per capita survival benefits ranged from 9.3-10.2 years across the 8 cohorts. Total population estimated lifetime survival benefit was 21.7 million life-years, of which 2.8 million life-years had been realized by December

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2012. By 2030 with increased linkage to care and universal second-line ART 28.0 million life-years could be realized.

■ COMMENTARY

As many as 5.6 million patients in South Africa are estimated to be infected with HIV using UN Programme on HIV/AIDS (UNAIDS) data. AIDS-related deaths exceeded 200,000 per year since 2001, reflecting a huge burden of human suffering. Beginning in about 2004 programs such as the US President's Emergency Plan for AIDS Relief (PEPFAR), other multilateral funding, and philanthropic funding (Bill and Melinda Gates Foundation) began making ART a reality for patients throughout many countries in sub-Saharan Africa, including South Africa. The particular modeling used in this study likely results in conservative estimates of survival benefits of ART. The profound survival benefits become even more impressive over the next 16 years if expanded linkage to care and treatment and universal second-line ART is provided. The model does not take into consideration the benefits of ART on prevention of secondary transmission ("treatment as prevention"), the benefits of prevention of mother-to-child transmission, nor the benefits of ART in children. If these were considered, the survival benefit of ART would be even larger.

In a related paper[1], 12 focus countries in Africa (countries receiving the greatest US investments) were compared to 29 nonfocus countries. Tuberculosis incidence, prevalence, and mortality rates were estimated before and after PEPFAR's inception. The relative risk for developing TB, comparing those with and without HIV, was 22.5 for control and 20.0 for focus countries, showing that PEPFAR had a consistent and substantial effect on HIV and TB incidence in focus countries. This highlights the likely link between high levels of investment in HIV care and the effects on diseases such as TB.

Reference

1. Lima VD, et al. Potential impact of the US President's Emergency Plan for AIDS Relief on the tuberculosis/HIV coepidemic in selected sub-Saharan African countries. *J Infect Dis* 2013; 208: 2075-84. ■

SPECIAL REPORT

Influenza in Severely Immunocompromised Patients

By Stan Deresinski, MD, FACP, FIDSA

Clinical Professor of Medicine, Stanford University, Hospital Epidemiologist, Sequoia Hospital, Redwood City, CA, Editor of Infectious Disease Alert

SYNOPSIS: Influenza virus infection in severely immunocompromised patients is associated with reduced initial symptoms, but increased risk of severe outcomes. Treatment options with good supportive evidence are limited.

SOURCES: Memoli MJ, et al. The natural history of influenza infection in the severely immunocompromised vs nonimmunocompromised hosts. *Clin Infect Dis* 2014; 8:214-24.

Ison MG. Influenza prevention and treatment in transplant recipients and immunocompromised hosts. *Influenza Other Respir Viruses* 2013;7:Suppl 3:60-6.

PREVENTION

The optimal approach to influenza is prevention but there are problems related to the immunogenicity of influenza vaccines in immunosuppressed transplant recipients, as indicated by Ison et al. There is a consensus that influenza vaccination does not lead to organ transplant rejection. Serological response to vaccination is, however, diminished in transplant patients when compared to non-immunocompromised individuals.

Very recent IDSA guidelines currently state the following regarding influenza vaccination.[1] "Annual vaccination with inactivated influenza vaccine (IIV) is recommended for immunocompromised patients aged >6 months, except for patients very unlikely to respond…such as those receiving intensive chemotherapy or those who have received anti-B-cell antibodies within 6 months." Allogeneic and autologous HSCT recipients should receive a single dose beginning 6 months after transplantation, but, in the context of a community outbreak of influenza, the first dose should be given at 4 months. Children 6 months to 8 years of age receiving IIV for the first time should receive 2 doses. A "double-dose" influenza vaccine has improved immunogenicity in the elderly, but whether it has similar benefit in immunocompromised patients, including transplant recipients, is not yet known.

Household members >6 months of age should be vaccinated with IIV. Live attenuated vaccine (LAIV) should not be given to members of the household of a hematopoietic stem cell recipient transplanted within the previous 2 months or with graft vs. host disease, or if the patient has severe combined immunodeficiency. If a household member receives LAIV, he or she should avoid contact with the patient for 7 days.

CLINICAL MANIFESTATIONS

Memoli and colleagues prospectively evaluated 32 severely immunocompromised and 54 non-immunocompromised adults with influenza virus infection in order to assess any differences in their clinical manifestations and course. Influenza vaccination had been received in the previous year in 59% and 25%, respectively. Nineteen (59.4%) of the immunocompromised patients had undergone hematopoietic stem cell transplantation (HSCT).

A dry cough was present in approximately three-fourths of the immunocompromised patients, as was coryza while 85.2% were febrile, 70.4% complained of headache, and 40.7% of myalgia. Many symptoms were less prevalent in the immunocompromised than in the nonimmunocompromised cohort. These included dry cough, chills, sweats, myalgia, and shortness of breath. All the immunocompromised patients were hospitalized and 6 (18%) required intensive care, including mechanical ventilation, while none of the nonimmunocompromised patients required intensive care, although 16 (29.6%) were hospitalized. One (3%) patient, who was immunocompromised, died.

The mean durations of viral shedding were 19.0 days and 6.4 days in immunocompromised and non-immunocompromised patients, respectively. Persistent shedding was often associated with a lack of symptoms. New chest radiographic abnormalities, often in the absence of physical findings, were present significantly more immunocompromised patients, although many of the comparator group did not undergo lung imaging. Two thirds of the viruses detected were A (H1N1)pdm09. Neuraminidase resistance occurred during neuraminidase inhibitor therapy in 3 cases. One H3N2 virus developed a novel mutation, while 2 A(H1N1)pdm09 viruses developed H275Y mutations. There was no difference in proinflammatory cytokine levels in nasal washes and serum between the two groups.

TREATMENT

Studies suggest that treatment of infection due to susceptible influenza virus with oseltamivir is associated with improved outcomes. The data in severely immunocompromised hosts is limited, but more is available regarding hospitalized and critically ill patients in general. For instance, a recent retrospective analysis found evidence of survival benefit in critically ill patients infected with A(H1N1)pdm09 when

oseltamivir administration was initiated as late as 5 days after symptom onset.[2]

There is limited data in immunodeficient patients with use of nebulized zanamivir. An intravenous form of zanamivir remains investigational, but non-randomized data suggests it is effective in the treatment of influenza A viruses with an H275Y associated with resistance to oseltamivir. This mutation is also associated with reduced susceptibility to peramivir, which is also under investigation as a parenterally administered agent.

Administration of intravenous peramivir produced clinical responses similar to that of oseltamivir in a randomized trial in hospitalized patients with influenza virus infection.[3] Lanamivir, a neuraminidase inhibitor active against oseltamivir-resistant influenza virus and which is administered as a single dose by inhalation, is in a Phase 3 trial. Favipravir (formerly T-705), which inhibits RNA-dependent RNA polymerase, is active against a spectrum of RNA viruses and is being evaluated in a Phase 3 trial in patients with uncomplicated influenza. In a very underpowered randomized trial, there was no difference in the duration of symptoms of patients infected with A(H1N1) pdm09 treated with either oseltamivir alone or together with zanamivir.[4] A retrospective analysis of critically ill patients requiring mechanical ventilation with A(H1N1)pdm09 infection concluded that a 3-drug combination of oseltamivir, amantadine, and ribavirin "was comparable to that of oseltamivir monotherapy."[5]

Administration of hyperimmune globulin derived from convalescent plasma of patients who had survived A(H1N1)pdm09 infection to patients with infection with this virus was associated with modestly improved survival.[6] A number of monoclonal antibodies are also under development.

DAS181 is a sialidase that cleaves terminal sialic acid residues on respiratory epithelial cells that are necessary for binding of influenza viruses. Administered by inhalation, it has in vivo activity against influenza A, including A(H1N1)pdm09, influenza B, and parainfluenza viruses types 1-3. Its administration was associated with reduced viral load in a Phase 2 trial.[7]

As the result of evidence suggesting that the lung injury in influenza virus pneumonia results from the inflammatory response, corticosteroids have been suggested as an adjunctive therapy, but available evidence does not suggest resulting benefit.

A number of additional anti-inflamatory molecules are under investigation.

Extracorporeal membrane oxygenation (ECMO) is increasingly being used as salvage therapy. A systematic review and meta-analysis of the use of ECMO in patients with acute lung injury in association with A(H1N1) pdm09 infection could only conclude that it is "feasible and effective," but that it is usually prolonged for > 7 days and the mortality remains high.[8] The conclusion that it is effective can be questioned since all included studies were only observational.

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ABSTRACT & COMMENTARY

Calcium-Channel Blocker-Clarithromycin Drug Interactions and Kidney Injury

By Richard R. Watkins, MD, MS, FACP

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Dr. Watkins reports no financial relationships in this field of study.

SYNOPSIS: In a retrospective cohort study, elderly patients who were prescribed calcium-channel blockers (CCBs) with clarithromycin were at increased risk for developing acute kidney injury. Moreover, all-cause mortality was greater with clarithromycin and CCB co-prescription (1.02%) vs. azithromycin and CCBs (0.59%). Co-prescription of CCBs and clarithromycin should be avoided.

SOURCE: Gandhi S, et al. Calcium-channel blocker-clarithromycin drug interactions and acute kidney injury *JAMA* 2013;310:2544-53.

Calcium channel blockers are a commonly prescribed class of medications for managing hypertension and are metabolized by the CYP3A4 enzyme. Pharmacokinetic studies have shown that coadministration of CYP3A4 inhibitors (e.g. erythromycin and fluconazole) with CCBs can raise serum CCB concentrations up to 500%, leading to associated toxicities such as excessive blood pressure lowering. The kidney is particularly susceptible to acute ischemic injury from hypotension and acute kidney injury often leads to increased morbidity, mortality and resource utilization. Gandhi and colleagues investigated the association between co-prescription of CCBs and clarithromycin with the development of acute kidney injury (AKI).

The study was a population-based, retrospective cohort of patients aged 65 years or older from June 2003 until March 2012 that used a health care database from Ontario, Canada. The investigators identified 96,226 patients who took a CCB along with clarithromycin and 94,083 who took a CCB with azithromycin as a comparison group. Baseline characteristics between the two groups were almost identical. The primary outcome measured was hospitalization with AKI and the secondary outcomes included hospitalization due to hypotension and all-cause mortality. All three outcomes were assessed within 30 days of the index date. Of note, the investigators were careful to have the dates covered by the CCB prescription overlap the dates covered by the antibiotic.

Co-prescribing clarithromycin with a CCB was associated with a higher risk for developing AKI (0.44% of patients) compared to azithromycin and a CCB (0.22%); odds ratio [OR], 1.98 [95% CI, 1.68-2.34]. Median doses of clarithromycin were similar among patients with and without chronic kidney disease. The risk for hospitalization from hypotension was greater among patients taking clarithromycin and a CCB (0.12% of patients) than with azithromycin and a CCB (0.07%); absolute risk increase, 0.04%; OR, 1.60 [95% CI, 1.18-2.16]. Among the CCBs, nifedipine (the most potent vasodilator) was associated with the highest risk. All-cause mortality was also higher in the clarithromycin/CCB group (1.02% of patients) vs the azithromycin/CCB group (0.59%); absolute risk increase, 0.43%; OR 1.74 [95% CI, 1.57-1.93]. Gandhi and colleagues also found that a higher dose of clarithromycin (1000 mg/d) co-prescribed with a CCB resulted in a higher risk for hospitalization with AKI (307 patients out of 28,591 taking a high dose [0.47%]

vs 95 out of 65,801 taking a low dose [0.33%]; absolute risk increase 0.13%; OR, 1.42 [95% CI, 1.13-1.79]. Finally, no significant difference was found in outcomes between patients who took clarithromycin vs azithromycin with a CCB at 90 days following the co-prescription.

■ COMMENTARY

This was an interesting study that showed a small but significant risk for developing AKI in older adults within 30 days of taking clarithromycin and a CCB. Although less commonly prescribed in clinical practice than other macrolides, clarithromycin still has many uses, for example, in combination therapy for nontuberculosis Mycobacterium and H. pylori infections. It is therefore important that prescribers be aware of the potential risks with clarithromycin and to carefully consider the potential for drug-drug interactions. Indeed, azithromycin has similar clinical indications to clarithromycin yet is a much less potent inhibitor of CYP3A4.

There were a few important limitations to the study. Because of the retrospective and observational design, the results may have been influenced by unmeasured confounding variables. Drug-drug interactions are complex and factors besides CYP34A enzyme inhibition may have also affected the results. Furthermore, older adults are more susceptible to both drug-drug interactions and AKI so the findings of the study may not be generalizable to other patient populations (i.e. younger patients). Finally, the circumstances for which clarithromycin was chosen over azithromycin were not ascertained, thus making it challenging to know the how much the illness being treated contributed to AKI and/or mortality.

Based on this study as well as prior data showing similar adverse events, I suggest that co-prescribing clarithromycin and CCBs be avoided whenever possible. Clinicians should either choose an alternative antibiotic that does not inhibit the CYP3A4 enzyme for a patient taking a CCB or else switch the CCB to an alternative anti-hypertensive agent for the duration of clarithromycin therapy. ■

SPECIAL REPORT

Arboviruses and Pacific Islands: Zika in Polynesia, Chikungunya in Micronesia, Dengue in Melanesia

By Stan Deresinski, MD, FACP, FIDSA

Clinical Professor of Medicine, Stanford University, Hospital Epidemiologist, Sequoia Hospital, Redwood City, CA, Editor of Infectious Disease Alert

SYNOPSIS: Arbovirus infections, including Zika, are currently a prominent cause of febrile illness in Pacific Islands nations.

Zika virus is a mosquito-borne flavivirus first identified in 1947 in a sentinel rhesus monkey stationed on a tree platform in the Zika forest, near Entebbe, Uganda.[1] The virus was subsequently isolated from a pool of Aedes africanus mosquitoes collected in 1948 from the same area of the forest. At the same time, a serosurvey found that 6.1% of the residents in nearby regions had specific antibodies to Zika virus.

In December 2013, the French Polynesia Department of Health confirmed an outbreak of Zika fever in the islands of Tahiti, Moorea, Raiatea, Tahaa, Bora Bora, Huahine, Nuku Hiva, Hiva Oa, Ua Pou, Hao, Rangiroa, Fakarava, Tikehau, Takaroa Ahe and Arutua.[2] By December 3,

2013, 99 laboratory confirmed cases and 35,000 suspected cases had been reported. No hospitalizations or deaths have been reported. It is estimated that 7.6% of the total population have had symptomatic infection that lasted, on average, 3-6 days. Rash was present in 95%, fever in 73%, arthralgia in 70%, and conjunctivitis in 43%. There has, at the same time, been a marked increase in cases of Guillian-Barre syndrome, approximately 8 times higher than expected, and each case had a previous illness compatible with Zika. However, no one was tested, so a link has not been demonstrated.

Only one previous large outbreak of Zika has been reported. In 2007, a relatively mild febrile illness with rash, conjunctivitis and arthralgia was recognized to be affecting residents of Yap, one of the Carolina islands of the Federated States of Micronesia. A total of 108 cases (49 proven, 59 probable) were identified. Although many patients had IgM antibody to dengue virus, the infection proved to be due to another flavivirus, Zika, which had previously only been reported in 14 individuals.[1,3] There were no hemorrhagic manifestations, hospitalizations, or deaths identified.

Chikungunya virus (which has recently made its first appearance in the Caribbean,[4] is now causing an ongoing outbreak of infection in Yap. As of November 29, 2013, there had been more than 1,000 suspected cases of infection with this alphavirus. No deaths had been reported. Dengue has been undergoing ongoing transmission in many areas of the Pacific, including Micronesia and the Solomon Islands, which is part of Melanesia.[5,6]

Dengue has been active in tropical and subtropical regions for many years and has recently extended its reach into areas of southern France and in Florida. Chikungunya has continued to be transmitted in vast areas surrounding the Indian Ocean, including southeast Asia, but has also extended its presence into places such as Italy and, now, the Pacfiic Islands. The outbreak of Zika virus infection in French Polynesia raises the profile of this obscure virus.

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ABSTRACT & COMMENTARY

Reducing Antibiotic Overuse: An Intervention with Positive Outcomes

By Leslie A. Hoffman, RN, PhD, Professor Emeritus, Nursing and Clinical & Translational Science, University of Pittsburgh

Dr. Hoffman reports no financial relationships in this field of study

SYNOPSIS: Active, daily communication between infectious disease and critical care practitioners significantly reduced antibiotic overuse without increasing mortality.

SOURCE: Rimawi RH, et al. Impact of regular collaboration between infectious diseases and critical care practitioners on antimicrobial utilization and patient outcome. *Crit Care Med* 2013;41:2099-2107.

This study was undertaken to test the potential that routine daily assessment of antibiotic use by an infectious disease (ID) specialist (fellow) could further improve

best practices for ICU patients. At the time the study was instituted, the institution had implemented an antimicrobial stewardship program and rounds included pharmacist consultation. However, chart reviews indicated "considerable opportunity" for improvement. Baseline data were collected during a 3-month preintervention period followed by the 3-month intervention that was scheduled 1 year after baseline data collection to avoid seasonal discrepancy. The ID fellow reviewed charts of all medical ICU (MICU) patients receiving antibiotic therapy, discussed complex cases with the ID attending, and rounded with the critical care team to provide recommendations. Antibiotic use was recorded as days of therapy. In this calculation, each antibiotic given on a single day was recorded as 1 day of therapy (DOT), i.e., 1 antibiotic/day = 1 DOT and 3 antibiotics/day = 3 DOT. DOTs were divided by length of stay (LOS); the ratio was multiplied by 1000 and expressed as DOT/1000 patient days to allow comparison between cohorts with differing LOS. Antibiotics given prior to MICU admission or after MICU discharge were not included.

A total of 246 charts were reviewed: 123 in the preintervention phase and 123 in the post-intervention phase. There were no significant between-group differences in age, gender, race, APACHE II scores, or types of infections. Fewer patients received antibiotics that did not correspond to guidelines during the intervention period ($P < 0.0001$). There was a significant reduction in antibiotic use during the intervention period (1590 vs 1420 DOT/1000 patient days; $P = 0.03274$). There was also a 17-fold increase in the use of narrow-spectrum penicillins (e.g., penicillin G and nafcillin) in the intervention phase (67 vs 4 DOT/1000 patient days; $P = 0.0322$). All-cause hospital mortality was significantly lower in the intervention phase ($P = 0.0367$) with no difference in all-cause MICU mortality ($P = 0.4970$). There was a significant reduction in days of mechanical ventilation (6.07 vs 10.1; $P = 0.0053$) and MICU LOS (7.78 vs 10.29; $P = 0.0188$) in the intervention period, compared to the preintervention period. Cost of antibiotics in the preintervention period exceeded that in the intervention period by a difference of $22,486.

■ COMMENTARY

Efforts to better match antibiotic prescriptions with patient needs are clearly warranted. In this institution, an antibiotic stewardship program had already been instituted. However, despite existence of this program and the inclusion of a pharmacist on rounds, there continued to be a need for improvement, based on chart reviews. The ID specialist made 180 recommendations during the 3-month course of the study. Specific recommendations related to shortening (n = 77), stopping (n = 53), narrowing (n = 34), or broadening therapy (n = 4), as well as converting to oral administration (n = 8) and changing therapy due to an adverse effect (n = 4). Thus, most (72%) recommendations related to more timely cessation of therapy.

The authors posed several reasons for this outcome. Rather than lack of knowledge, they suggested that reluctance to change therapy was potentially related to hesitation to abruptly change antibiotics after a handoff of care, even when there was awareness that a change was indicated, until familiar with the case. Because the ID specialist was actively involved in discussions during MICU rounds, there could be "consensus discussions" leading to change. When proposing the intervention, there was concern that disputes might arise between specialties. This did not occur and the volume of ID consultations was not affected.

When calculating cost saving, the analysis only considered hospital pharmaceutical acquisition costs. No costs were attributed to the ID specialist, who was a fellow, since the experience was considered part of training. The time requirement for providing consultation (estimated at 2 hours/day) was not excessive and the experience was judged an excellent academic fellowship opportunity. The study, therefore, met its goal of achieving better antibiotic stewardship with no untoward consequences. The benefits of an ID specialist participating in rounds on patients with sepsis on clinical units have been well documented. The current study extends these benefits to the ICU setting. ■

Overcoming barriers to HPV vaccine

By Anita Brakman, MS, Senior Director of Education, Research & Training, Physicians for Reproductive Health, New York City

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The authors report no financial relationships in this field of study.

In June 2013, researchers reported that the vaccine for human papillomavirus (HPV) effectively reduces infection with high risk strains of the virus among female adolescents ages 14-19. The study reveals that since the first vaccine was introduced in 2006, vaccine-type HPV prevalence among this population of young women has decreased by 56%.[1] Despite this encouraging news, the introduction of a second vaccine, and recommendations for routine vaccination of young females and males starting at ages 11 or 12, many adolescents and young adults remain unprotected.

The 2012 National Immunization Survey — Teen found that a little more than half (54%) of U.S. females ages 13-17 had received at least one dose of vaccine and only 33% had completed all three doses in the series. Coverage was worse among males in the same age group compared to females, with only 21% starting the series and 7% completing three doses.[2]

A November 2013 review in JAMA Pediatrics examined why coverage remains low and identified several key barriers that contribute to lower vaccination coverage rates compared to other vaccines recommended for adolescents. The review included articles published between 2009 and 2012 with the sole focus being barriers to HPV vaccine initiation or series completion among U.S. adolescents ages 11-17. Most of the articles addressed barriers experienced by parents, and the authors also assessed barriers experienced by healthcare professionals, historically underserved populations, and males.[3]

Most parents in the included studies were aware of the vaccine but desired more information and reported knowledge gaps as a barrier. Many studies found parents were concerned about the vaccines' relative newness and potential adverse effects or safety, but it was not clear if these concerns actually inhibited uptake. A small group of parents across studies reported concerns about the vaccines' potential to increase sexual activity among adolescents, though this fear has not been proven to be true. In 2012, a retrospective cohort study of nearly 1,400 female adolescents found no increase in testing or diagnosis of sexually transmitted infections or pregnancy and no increase in requests for contraceptives among those who initiated vaccination compared to unvaccinated teens.[4] The review found mixed results when looking at parental religious beliefs as a barrier to vaccination.

WHAT INFLUENCES PARENTS?

Factors that were associated with vaccine acceptance among parents included receiving a doctor's recommendation, perceived risk of HPV-related disease, belief that the vaccine was part of a social norm, as well as a history of seeking other preventive services. Additionally, not receiving a doctor's recommendation was associated with non-initiation.[3]

Articles examining healthcare professionals found a variety of barriers in place. Several studies found clinicians reported a lack of knowledge about the relationship between HPV and urogenital or oral cancers, which indicates an ongoing need for medical education on this topic. Additionally, many providers reported recommending the vaccine only to select populations. Some offered vaccination only to those they perceived as high risk (often low income and/or patients of color). Others reported age or gender biases and only vaccinated older teens or females, but not males. Some questioned the cost effectiveness of vaccinating young males.[3]

While increasing vaccine coverage among females is a more efficient strategy than vaccinating males overall, providing the vaccine to young men is cost effective when vaccine

coverage rates among young women are low and when all potential HPV vaccine-related benefits are included in analysis. Considering reductions in oropharyngeal cancers, penile cancer and recurrent respiratory papillomatosis in addition to reduced cervical, vaginal, vulvar, and anal cancers, and genital warts when analyzing benefits of the vaccine will demonstrate more significant cost benefits to the expanded recommendation for routine vaccination for both young females and males.[5]

Understanding this data makes it clear that clinicians have a significant role to play in increasing HPV vaccination rates to further decrease prevalence of high risk HPV strains.

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Infectious Disease [ALERT]

Updates

By Carol A. Kemper, MD, FACP

Religious deterrence?

Van Wagoner N, Et al. *Clin Infect Dis* 2014; 58(2):295-9.

A cross-sectional analysis of persons newly presenting for HIV care was performed at a University HIV clinic in Alabama GA, examining risk factors for delayed presentation. Part of the initial intake was an assessment of church attendance, which was compared with self-reported sexual behavior (including men who have sex with men [MSM], men who have sex with women [MSW], and women who have sex with men [WSM] — men who have sex with both were included in MSM). A total of 508 people were included in the survey (60% MSM, 21% MSW, and 18%WSM). The median age was 33 yrs; and 62% were African American. More than half (56%) attended church on a regular basis. One-third had a CD4 count < 200 cells/mm3 (AIDS by CD4 count) at presentation.

There was a statistically significant correlation observed between church attendance and presentation with AIDS (p=.02). Church-going MSM were statistically more likely to present with more advanced disease, as defined by CD4 count < 200 cells/mm3, than non-church goers (34% vs 20%, adjusted OR = 2.2, p= .01). Church-going MSM were also statistically less likely to have been previously HIV tested (79% vs 88%, p = .041). The opposite was observed in WSM. Non-church going women were less likely to report prior HIV testing than church-going women (41% vs 68%, p=.01).

I suspect very different results might be observed if this analysis were performed in a part of the country other than the South, and the type of religion may have some bearing on the results. Nonetheless, I have heard many time from several of my black HIV+ MSM their concerns about being ostracized from their community, should their HIV+ status be revealed. ■

Average survival time of chocolate: 55 min

Gajendragadkar PR, et al. *BMJ* 2013; 347:f7198.

I love being on call for the Holidays — it's not so busy, and there are goodies and boxes of See's chocolate at every nursing station (despite our Infection Control provision against having food at the nursing station, which is largely ignored, especially at the holidays). It's no wonder

Warren Buffet bought See's candies in 1972.

These rascals in the Department of Cardiology at Bedford Hospital in the United Kingdom surveyed the rate of chocolate consumption on nursing units at 3 different hospitals. Two different types of boxed chocolates were deployed (a total of 8 boxes, 2 per unit, with a total of 258 chocolates). The boxes were "kept under covert surveillance", and the time to consumption recorded. Three-fourths of the chocolates were observed being eaten.

The medium time to opening the first box of chocolate, once it arrived at the nursing station, was 12 minutes (range, 0 to 25 minutes). The average survival time of chocolate was 55 minutes. Chocolate consumption was non-linear, with a burst of chocolate eating activity followed by slower ingestion. Using an exponential decay model, the survival half-life for a box of chocolates was 99 minutes. One brand of chocolates survived longer than the other. Nurses and health care assistants consumed most of the chocolates, while only 15% fell victim to physicians. ■

Non-Medical Exemptions in California Contributing to Pertussis

There were more cases of pertussis reported to the California Department of Public Health in 2010 than in the previous 50 years. The CDPH collects data on confirmed, probable and suspect cases of pertussis (a total of 9143 such cases were reported in 2010). A confirmed or suspect case is defined as cough illness > 2 weeks and > 1 week of paroxysms of cough, inspiratory whoop, or posttussive vomiting, with confirmation by Bordetella pertussis PCR, or a consistent cough illness epidemiologically linked to a confirmed case.

Reported pertussis cases in 2010 varied from <100 cases in January to >1000 cases in August. Data on gender, race, ethnicity, and address was examined and "geocoded" for a geographic cluster analysis. A total of 39 geographic clusters of pertussis cases were identified (using SatScan). Two of the largest clusters spanned several months, including a cluster of 880 cases in San Diego County from July to November, and 3,783 cases in Central California from May to October.

This geographic cluster analysis of pertussis cases was then compared with census tract data, and school data for non-medical exemptions for pertussis vaccination. Specifically, medical exemption and non-medical exemptions (NME) for children starting kindergarten between 2005-2010 was collected. ME/NME data is publically available for any public school with 10 or more children. NME exemptions increased from 1.6% during the 2005-2006 school year to 2.4% in the 2009-2010 school year. Clusters of pertussis cases were 2.5 times more likely to occur in area of higher NME. Geographic areas with both clusters of pertussis cases and higher rates of NME were associated with factors suggesting higher socioeconomic status, including higher medium income, lower population density, fewer children within a family, and lower incidence of minorities.

These findings suggest that geographic areas with greater numbers of pertussis cases also have a higher than expected rates of non-medical exemption from vaccination. In other words, it directly points the finger at parents who decline vaccination for their children, as partly responsible for the current resurgence of pertussis in their community. Data suggests that at least 85% of the population must have existing immunity to thwart sustained transmission of diseases like pertussis and measles. Although the process for medical and non-medical exemption from vaccination is apparently more difficult in other states, California requires only a signed form from a parent, indicating non-medical philosophical or religious exemptions in a category called "personal belief exemption". No physician consultation or input is required. ■

Atwell, JE et al. Nonmedical vaccine exemptions and pertussis in California, 2010. *Pediatrics* 2013; 132: 624-630.

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 **www.cmecity.com** to take a post-test; tests can be taken after each issue or collectively at the end of the semester. 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 last test of the semester, 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. Which of the following is correct with regard to antiretroviral therapy (ART)?

A. The introduction of ART has been ineffective in Africa because of lack of patient compliance.
B. The introduction of ART in Africa has been associated with an estimated life-time survival benefit of almost 22 million life-years.
C. The introduction of ART in Africa has been associated with an estimated life-time survival benefit of almost 53 million life-years.
D. The introduction of ART in Africa has been associated with an estimated life-time survival benefit of less than 2 million life-years.

2. Which of the following is correct with regard to influenza virus infection and the immunocompromised patients?

A. Influenza vaccination should be avoided in transplant recipients because it causes organ rejection.
B. Despite greater severity of illness, the duration of influenza virus excretion was briefer in immunocompromised than in immunocompetent patients.
C. Myalgias occurred less frequently in immunocompromised than in immunocompetent patients.
D. Prednisone administration has clearly been demonstrated to improve survival.

3. Which of the following is correct?

A. Coadministration of erythromycin with a calcium channel blocker such as nifedipine, can result in a 500% increase in serum concentrations of erythromycin.
B. Exposure to excessive concentrations of calcium channel blockers may lead to renal dysfunction as result of such concentrations causing elevated blood pressure.
C. Coadministration of clarithromycin with a calcium channel blocker such as nifedipine, results in an increased risk of diarrhea due to elevated serum concentrations of the antibiotic.
D. Coadministration of clarithromycin with a calcium channel blocker such as nifedipine is associated with an increased risk of acute kidney injury, hospitalization because of hypotension, and all-cause mortality.

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 latent 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

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[IN FUTURE ISSUES]

Protective Association Between Rotavirus Vaccination and Childhood Seizures in the Year Following Vaccination in US Children

Appropriate Antibiotic use for Patients with Urinary Tract Infections Reduces Length of Hospital Stay

Searching for an Optimal Hand Hygiene Bundle: A Meta-analysis