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New Recommendations for 13-Valent Pneumo Vaccine in Compromised Adults

ABSTRACT & COMMENTARY

By Mary-Louise Scully M.D.

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Dr. Scully reports no financial relationships to this field of study

Synopsis: *New recommendations have been approved for the use of 13-valent pneumococcal conjugate vaccine in conjunction with the 23-valent-polysaccharide pneumococcal vaccine in immunocompromised adults ages 19 and older.*

Source: Centers for Disease Control and Prevention, Advisory Committee on Immunization Practices (ACIP). June 20-21 2012 (slide presentations). Atlanta Georgia http://www.cdc.gov/vaccines/recs/acip/slides-jun12.htm#pcv accessed July 7, 2012.

At the June 20, 2012 meeting in Atlanta, Georgia the CDC Advisory Committee on Immunization Practices [ACIP] voted in favor of recommending the addition of 13-valent pneumococcal conjugate vaccine (PCV13) to the 23-valent pneumococcal polysaccharide vaccine (PPSV23) for adults aged 19 and older with immunocompromising conditions. PCV13 was licensed in December 2011 for use among adults ≥50 years of age based on non-inferior immunogenicity compared to PPSV23. The serotypes in PCV13 include serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.

The indications are for adults 19 years of age or older with immunocompromising conditions. They include HIV infections, chronic renal failure, malignancies, leukemias, lymphomas, multiple myeloma, Hodgkin's disease, immunosuppressive drugs, solid organ transplants, congenital or acquired immunodeficiencies, functional or anatomic asplenia and patients with CSF leaks or cochlear implants. The categories are divided into vaccine naïve versus previously PPSV23- immunized.

1. For pneumococcal vaccine naïve patients it is recommended that PCV13 be given before PPSV23 whenever possible. After a single dose of PCV13 is given, a dose of PPSV23 should be given at least 8 weeks after PCV13. Another dose of PPSV23 can then be given 5 years later, and at age 65.

2. Patients previously immunized with one or more doses of PPSV23 should receive 1 dose of PCV13 given at least 1 or more years after the last PPSV23 dose was received. In situations where a patient needs additional doses of PPSV23 according to the previous guidelines, the next dose of PPSV23 should be at least 8 weeks after PCV13, and at least 5 years after the most recent dose of PPSV23.

The PCV13 is currently licensed for children aged 6 weeks through 71 months and adults aged 50 years and older. Therefore, it should be noted that for persons aged 19-49 years, this is an off-label use of the PCV13 vaccine.

■ COMMENTARY

Vaccine strategies continue to emerge in attempts to reduce the morbidity and mortality of pneumococcal disease in both children and adults. Before universal infant immunization with pneumococcal 7-valent conjugate vaccine (PCV7) in the United States, *Streptococcus pneumoniae* was estimated to cause over 17,000 cases of invasive pneumococcal disease (IPD) among children < 5 years of age, including 800 cases of meningitis and 200 deaths.[1] The routine use of PCV7 essentially eliminated IPD secondary to serotypes included in the vaccine both in children and also in adults due to herd immunity. There was an increase in the proportion of cases of IPD caused by non-vaccine serotypes, or so-called replacement strains, but this increase was small compared to the overall decline in numbers of IPD (net decline of 24,878 cases).[2] When PCV13 replaced PCV7 in 2010 for routine childhood use, certain troublesome serotypes such as, serotype 19A, which had emerged as an important cause of multidrug resistant *otitis media* in children, were included in newer PCV13 vaccine. The looming question is whether the routine use of PCV13 in children will also reduce IPD from these vaccine serotypes in adults, similar to what was observed after the introduction of PCV7, which lead to a near elimination of vaccine serotype IPD in adults of all age groups.

Although this recommendation for use of PCV13 in immunocompromised patients was approved, the decision on the routine use of PCV13 in adults over 50 years will likely depend on evolving data and the results of a randomized, controlled trial ongoing in the Netherlands. Since, for patients 19-49 years of age, PCV13 vaccine represents off label use, there may be issues about insurance reimbursement for the vaccine. Patients meeting the new guidelines directives may therefore have "out of pocket" costs similar to what many patients experienced with the initial licensing of the Herpes zoster (shingles) vaccine. The cost per dose of PCV13 in the private sector is about $120 US dollars. This is a price that some immunocompromised patients, with the available financial means, might be willing to pay to reduce their risk of pneumococcal disease.

References

1. CDC. Preventing Pneumococcal Disease among Infants and Young Children: Recommendation of the ACIP. *MMWR* 2000;49(No. RR-9):1-35.
2. CDC. Direct and Indirect Effects of Routine Vaccination of

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Children with 7-valent Pneumococcal Conjugate Vaccine on Incidence of Invasive Pneumococcal Disease – United States – 1998-2003. MMWR 2005;54(36): 893-897. ■

Travel-Related Problems in Children

ABSTRACT & COMMENTARY

By Philip R. Fischer MD, DTM&H

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Dr. Fischer reports no financial relationships to this field of study.

Synopsis: *Bothersome minor ailments are common in pediatric travelers. Serious health problems are uncommon and often preventable.*

Sources: van Rijn SD, et al. Travel-related morbidity in children: a prospective observational study. *J Travel Med* 2012;19: 144-149.

Herbinger KH, et al. Spectrum of imported infectious diseases among children and adolescents returning from the Tropics and Subtropics. *J Travel Med* 2012;19:150-157.

Hunziker T, et al. Profile of travel-associated illness in children, Zurich, Switzerland. *J Travel Med* 2012;19:158-162.

■ SUMMARY

These three papers and an accompanying editorial[1] in a recent issue of the *Journal of Travel Medicine* form a mini-symposium on pediatric travel medicine. Each gives a glimpse of problems experienced by children traveling internationally and nicely contributes to the limited literature on this topic.

van Rijn and her group in the Netherlands had 152 pediatric travelers aged 0 to 18 years and their parents prospectively track ailments during their international trips, ranging from one to nine weeks in duration. The tracking survey recorded the presence or absence of 33 specific "ailments." Prior to departure, already-active common ailments included insect bites (11% of children), diarrhea (9%), and earache (8%). The incidence of ailments increased approximately three-fold during travel with 40% reporting insect bites, 30% having diarrhea, 27% having fatigue, and 19% having sunburn. Only 1.5% of children had an ailment serious enough to prompt a visit to a doctor or clinic, with common cold, nausea, fatigue, abdominal pain, and insect bites being the most common reasons to seek medical care. No serious illness was identified in this cohort of traveling children who had received pre-travel care.

Herbinger and his colleagues in Germany reviewed 890 pediatric travelers (<20 years of age) who had received post-travel care during a 20-year period following travel to tropical and subtropical areas. 87% were German-born, although nearly one-third of those were traveling to visit friends and relatives, and 46% were traveling to Africa. Diarrhea was reported by 25% and was most common in preschool-aged children. Skin problems (21% of returned travelers), febrile illness (20%), and respiratory problems (8%) were other commonly-identified diagnostic categories. Two percent of travelers had malaria. Young age and sub-Saharan African destinations were associated with increased risk of acquiring infections.

Hunziker and his Swiss colleagues reviewed findings in a group of 328 children, 0-16 years of age, who sought post-travel care for a presumed travel-related illness. About half were tourists, and about half had traveled to visit friends and relatives. Eleven percent required hospitalization, and there were no deaths reported. Diarrhea was seen in 39%, and increasing age was associated with an increased risk of acquiring diarrhea. Respiratory illness accounted for 29% of these post-travel consultations, and systemic febrile illness was seen in 13% of patients. Eleven of 12 children with "potentially serious diagnoses" (including malaria, typhoid infection, meningitis, tuberculosis, and hepatitis A) had been traveling to visit friends and relatives.

■ COMMENTARY

Each of these studies provides helpful information for our understanding risks to pediatric travelers. The Dutch study reminds us that common minor conditions occur more frequently during travel, and point to the necessity of continuing to include advice about hygiene (food, water, and hand) and skin protection (insect repellents and sunscreen) in pre-travel consultations. Interestingly, though, all these children had received pre-travel care, hence improved compliance with the pre-travel advice provided is still needed.

The German and Swiss post-travel studies remind us that travel-related infectious illnesses still account for serious disease in children who have

successfully returned home after international trips. Some of these conditions (specifically malaria, diarrhea, typhoid, and hepatitis A) are potentially preventable. The frequency of illness in German and Swiss children who had traveled to see friends and relatives reminds us of the ongoing importance of providing useful pre-travel interventions to this group. Knowing that about 10% of international travelers are children, Greek investigators noted that only 3% of their pre-travel consultations were for children;[2] there is still need to provide access to pre-trip interventions for children.

All three of these studies remind us that most children travel well without major health problems.[1] Especially with good pre-travel care, we should not be afraid to allow children to experience the many benefits of international travel.

There are, however, rare but catastrophic risks of travel. Injury was not reported in these studies, and no deaths were reported. One of the mainstays of pediatric pre-travel consultation is to provide guidance about safety and injury prevention. Devastating motor vehicle accidents and water-related trauma are rare, but are often preventable and would not have been identified in the German and Swiss studies of post-travel consultations. Pre-travel consultations should also include advice about appropriate use of safety restraints in motor vehicles, pedestrian safety, and safe water activity.

References

1. Neumann K. Pediatric travel medicine: where we are and where we hope to go. *J Travel Med* 2012;19:137-139.

2. Maltezou HC, et al. Pediatric international travelers from Greece: characteristics and pre-travel recommendations. *Travel Med Infect Dis* 2012;10:135-139. ■

Adequacy of Rabies Post-exposure Prophylaxis

By Lin H. Chen, MD.

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Dr. Chen has received research grants from the Centers for Disease Control and Prevention and Xcellerex.

Synopsis: *Travelers who experience animal bites often also experience delays in obtaining post-exposure prophylaxis, especially delays in obtaining human rabies immune globulin [HRIG]. Some develop suboptimal post-vaccination rabies antibody titers. Pre-travel advice needs to address ways to avoid these potential risks for rabies after bites which occur while overseas.*

Source: Uwanyiligira M, et al. Rabies post-exposure prophylaxis in routine practice in view of the new centers for disease control and prevention and world health organization recommendations. *Clin Infect Dis* 2012 Jul;55(2):201-5.

Uwanyiligira et al retrospectively analyzed charts of all patients seen at the Travel Clinic of the University Hospital in Lausanne, Switzerland, for rabies post-exposure prophylaxis (PEP) between January 2005 and August 2011. The study identified 110 patients, including 90 travellers. Their median age was 34 years (range, 2–79 years), and 53% were women. Of the 90 travelers with possible rabies exposure overseas, 54 sought evaluation at their destination, but 36 waited to obtain medical care until after return to Switzerland. Those who waited to obtain medical care in Switzerland had a median delay of 10 days (range 0-481 days) whereas those who started rabies PEP overseas had a median delay of 0 days (range 0-14 days).

All those who waited to initiate PEP in Switzerland received HRIG, but only 7/50 (14%) who initiated PEP overseas received HRIG. The countries where travelers received HRIG were Tunisia, Algeria, Thailand, Vietnam, Indonesia, and Brazil. However, HRIG administration was inconsistent in these countries because many other patients did not receive it.

There were 11 patients who received pre-exposure prophylaxis (PrEP) and rapid fluorescent focus inhibition tests (RFFIT) were done in these patients after the 2 post-exposure doses. Their geometric mean titer was 18.2 IU/ml (range 5.4-33.9 IU/ml). For 85 of the nonimmune patients, serology was obtained between 21-29 days after the 4th dose of rabies PEP. Their geometric mean titer was 3.7 IU/ml (range 0.1-38 IU/ml). Six of 90 previously unvaccinated patients had titers <0.5 IU/ml.

■ COMMENTARY

The GeoSentinel Surveillance Network analysis of 23,509 ill travelers seen from January 1998–May 2005 found 1.4% of the records indicated animal injuries That required rabies PEP.[1] The highest risk for exposure was travel to Asia (67% of cases), with Thailand, India, Indonesia, China, Nepal and

Vietnam being leading countries where exposure occurred.[1] Dogs were the main culprits (51%), followed by monkeys (21%) and cats (8%); the most common reason for travel was tourism.[1] Most of the cases involved short-term travel: 12% travelled for <7 days, 53% travelled for <28 days, and 85% for <3 months, and their median trip duration was 23 days.[1]

Similarly, another study of 139 patients treated for possible rabies exposure at the Rabies PEP Service in the Liverpool School of Tropical Medicine from 2000 to 2009 found Thailand and Turkey to be the most common countries of exposure (22.3% of cases each).[2] Dogs were also responsible for most bites (49.6%), and the majority of patients (63%) were aged 20-50 years.[2] Only 3 of 78 (3.8%) of those needing rabies immunoglobulin (RIG) per UK guidelines received it while overseas and only 11 more patients received RIG on return to the UK; delay in care was also documented.[2] Only 14 (10.1%) had received PrEP.[2]

Gautret et al reviewed 22 published rabies cases occurring travellers (tourists, expatriates and migrants) within the past decade, including 3 cases following short-term travel (≤2 weeks).[3] Their review determined that expatriates were better vaccinated than tourists (31% vs. 12%) before travel.[3] The risk of bite with potential rabies exposure is estimated at 0.4% of travelers per month of stay in a rabies-endemic country.[3]

A survey of German travel health advisors confirmed the emphasis on PrEP for expatriates where nearly all responders indicated that they would discuss the risk of rabies and preventive measures to long-term travelers and tourists planning to visit rural areas.[4] However, only 35-60% of the advisors would provide this information to travellers on package tours or visiting urban centers or to business travelers.[4] Clearly, improvement is needed in proper post-exposure management to persons who had PrEP as well as in reducing the inappropriate withholding of PEP in cases where treatment had been initially delayed.[4]

Uwanyilijira et al proposed measuring antibody levels on day 21 of the Essen PEP regimen to ascertain an adequate immune response. In an editorial, Wilde et al pointed out that few or no laboratories in rabies endemic countries can perform appropriate serology.[5] Furthermore, failure to obtain PEP frequently is due to high cost of rabies vaccine and HRIG. Therefore, reducing the amount of rabies vaccine needed would contribute to better follow through with PEP, along with reducing the duration to initiation of PEP.[5] They noted that modern high-quality equine rabies immune globulin produced in France, Thailand, China, and India are available in some rabies-endemic countries. This information is reassuring, though difficult in practice for travellers to determine the quality of the product they receive in endemic countries. Also, Uwanyilijira et al have shown the inconsistent use of rabies immune globulin in a number of countries.

This study has raised questions regarding adequacy of the reduced-dose Essen PEP with 4 doses of rabies vaccine, based on the suboptimal antibody levels (<0.5 IU/mL) in 6 of 90 patients (6.7%) following 4 doses. The authors have also identified the additional problems of delayed initiation of PEP in travelers who waited to obtain medical treatment after returning to Switzerland. Also only 7 of 50 travelers (14%) for whom HRIG was indicated had received HRIG while abroad. Travel medicine specialists should incorporate this information into pre-travel advice by informing travellers to seek proper post-bite care as soon as possible and to emphasize the importance of HRIG in addition to rabies vaccination.

References

1. Gautret P, et al. GeoSentinel Surveillance Network. Animal-associated injuries and related diseases among returned travellers: a review of the GeoSentinel Surveillance Network. *Vaccine*. 2007 Mar 30;25(14):2656-63.
2. Wijaya L, Ford L, Lalloo D. Rabies postexposure prophylaxis in a UK travel clinic: ten years' experience. *J Travel Med* 2011 Jul-Aug;18(4):257-61.
3. Gautret P, Parola P. Rabies vaccination for international travelers. *Vaccine* 2012:5;30(2):126-33.
4. Ross RS, Wolters B, Viazov SO, Roggendorf M. Awareness of rabies risks and knowledge about preventive measures among experienced German travel health advisors. *J Travel Med* 2006;13(5):261-7.
5. Wilde H. Editorial commentary: Rabies postexposure vaccination: are antibody responses adequate? *Clin Infect Dis* 2012;Jul;55(2):206-8. ■

Neglected Tropical Diseases: Nigeria at a Crossroads

By Brian G. Blackburn, MD and Michele Barry, MD FACP

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Drs. Blackburn and Barry report no financial relationships to this field of study.

Synopsis: *Among African nations, Nigeria contains the greatest number of people infected with neglected tropical diseases (NTDs). Nigeria has made many gains and possesses sufficient resources for NTD control and elimination campaigns, but governmental and non-governmental organizations must continue to move these programs forward and expand to a national scale.*

Source: Hotez PJ, et al. Nigeria: "ground zero" for the high prevalence neglected tropical diseases. *PloS Negl Trop Dis* 2012;6(7):e1600. doi:10.1371/journal.pntd.0001600

NTDs are a group of infectious diseases that are common among the world's poorest people. Endemic to many developing countries, the NTDs not only stem from poverty, but contribute to its perpetuation. Taken together, the burden of NTDs is greater than malaria or tuberculosis, and NTDs trail only pneumonia, HIV-AIDS, and diarrheal diseases as the leading infectious causes of disability-adjusted life years (DALYs) lost globally.[1] Although the global budget available to combat NTDs is far lower than for these other infectious diseases, advocacy and funding for NTDs has increased dramatically over the past decade, and is perhaps at its highest level ever. Control and elimination programs, often employing mass drug administration (MDA), have made great strides in lowering the prevalence of these diseases in many areas.

Globally, Africa bears the greatest NTD burden. This review highlights Nigeria, the most populous country in Africa, and containing 20% of its population, which bears the greatest burden of these diseases on that continent. Among the "high-prevalence" NTDs and those controlled by mass drug administration [MDA] programs are soil-transmitted helminths [ascariasis, trichuriasis, hookworm; the soil transmitted helminthes [STHs], lymphatic filariasis [LF], schistosomiasis, onchocerciasis, and trachoma. Nigeria has the highest prevalence in Africa for nearly all of these diseases (*see table, p. 59*), and is near the top globally. For both onchocerciasis and schistosomiasis, Nigeria has the highest prevalence in the world. These diseases place an enormous burden on Nigeria, and Africa as a whole. In addition to the direct morbidity and mortality for individuals infected with them, they adversely affect maternal-child health and worker productivity, in turn adversely impacting Nigeria's economy and perpetuating the cycle of poverty that so many of the patients infected with these diseases face.

Control and elimination programs for these NTDs utilize low cost, "rapid-impact" packages of drugs. Integrated control efforts can target all of these diseases simultaneously with the same infrastructure, thus saving resources - the cost in Africa to combine MDA programs for STHs, LF, onchocerciasis, schistosomiasis, and trachoma is less than US $1 per person annually. With such a program implemented on a national scale, LF, onchocerciasis, and trachoma could possibly be eliminated, and the prevalence of the STHs and schistosomiasis could be reduced substantially. For all of Nigeria, this would probably cost less than US $100 million annually. Because these NTDs actually cause poverty, the economic rate of return for integrated NTD control and elimination would likely be substantial.

Nigeria possesses many resources, with an economy that is Africa's third-largest and ranks 32nd globally. The annual GDP of Nigeria is over US $300 billion, and growing 7-8% per year. However, Nigeria's economy has increasingly depended upon oil - it is now one of the world's leading producers. Unfortunately, oil dependence has led to decreasing diversification, in turn resulting in high rates of youth unemployment and job insecurity. Despite the large financial resources, Nigeria ranks only 158th globally in the human development index (HDI). Between 1990 and 2006, Nigeria regressed in several development indices such as access to safe water and sanitation for its residents.

Encouragingly, Nigeria has made recent gains in NTD control and elimination. Guinea worm (dracunculiasis) cases have decreased from 3.3 million in 1986 (75% of the world's cases at the time) to zero, with the cessation of autochthonous transmission in 2009. Nigeria was scheduled to treat between 3 - 5 million people in 2011 with azithromycin through their trachoma control and elimination program. Over 95% of the 35,000 Nigerian communities at-risk for onchocerciasis have received annual mass ivermectin administration, and transmission has been interrupted in several locales. In Plateau and Nasarawa states in central Nigeria, ongoing ivermectin/albendazole MDA programs have resulted in reductions of onchocercal nodules by 95%, and LF prevalence by 83%. Schistosomiasis control is now being integrated with LF and onchocerciasis elimination campaigns, with six states now receiving targeted praziquantel mass drug administration.

Many of these gains have occurred in collaboration with the World Health Organization (WHO), UNICEF-Nigeria, the Carter Center's Nigeria office, the African Programme for On-

chocerciasis Control, and other governmental and non-governmental organizations (NGOs). Nevertheless, much of the Nigerian population still lacks access to the medicines essential for control of these infectious diseases. In 2009, a Nigerian ministry of health program for national NTD control and elimination was initiated. This program focuses on integrated and cost-effective approaches to control / eliminate LF, onchocerciasis, schistosomiasis, STHs, trachoma, leprosy, Buruli ulcer, human African trypanosomiasis, and guinea worm disease.

Nigeria has sufficient wealth and resources to mount an aggressive national campaign for control and elimination of NTDs. It would cost less than 0.1% of the Nigerian GDP to annually target the "high prevalence" NTDs through integrated MDA for STHs, LF, onchocerciasis, and schistosomiasis, possibly along with distribution of long-lasting insecticide-treated bednets, that would target both LF and malaria, as well as the SAFE (surgery, azithromycin, antibiotics, facial cleanliness, and environmental control) strategy for trachoma elimination. Integration of control and elimination programs is clearly the way forward, as this has been shown to decrease costs, improve coverage of these interventions, and makes logistical sense for these diseases which share such similar control and elimination strategies and logistics.[2,3] Another key need that must be addressed early in these efforts is to accelerate completion of NTD mapping nationally, so that efforts may be targeted appropriately.

Although the cost of these programs could, at first glance, appear to be a deterrent to Nigerian policy makers, the low proportional cost and expected acceleration of economic development that would result should offset these fears and result in increased advocacy and movement on the political agenda. A national NTD control and elimination program in Nigeria, in conjunction with better access to clean water and sanitation, would strengthen health systems and represent a highly effective pro-poor strategy. Though Nigeria may have a larger population and more resources than most of its neighbors, it can serve as a model for other African countries to follow.

References

1. Hotez PJ, et al. Control of Neglected Tropical Diseases. *N Engl J Med* 2007;357:1018-27.

2. Brady MA, et al. Projected benefits from integrating NTD programs in sub-Saharan Africa. *Trends Parasitol* 2006;22:285-91.

3. Blackburn BG, Eigege A, Gotau H, et. al. Successful integration of insecticide-treated bednet distribution with mass drug administration in Central Nigeria. *Am J Trop Med Hyg* 2006;75:650-655. ■

Ranking of Nigeria by neglected tropical diseases cases and prevalance

Disease	Estimated Number of cases in Nigeria	Ranking in Africa	Percentage of Global Disease Burden	Ranking Globally
Ascariasis	55 million	1	7%	5th behind India, Indonesia, China, and Bangladesh
Hookworm	38 million	1	7%	Tied for 4th with China behind India, Indonesia, and Bangladesh
Trichuriasis	34 million	1	6%	4th behind India, Indonesia, and Bangladesh
Schistosomiasis	29 million	1	14%	1
Lymphatic filariasis	• 25 million • 80–121 million estimated at risk, requiring mass drug administration	1	21%	3rd
Onchocerciasis	30 million at risk, requiring mass drug administration	1	36%	1
Trachoma	18 million at risk	Not determined	Not determined	Not determined

CME Objectives & Instructions

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

- discuss the latest data regarding the diagnosis and treatment of various travel-related diseases;
- explain new data concerning recommended precautions and prophylaxis for patients traveling to specific areas of the world;
- implement strategies in the practice setting to inform patients of disease outbreaks and epidemics relevant to their travel plans.

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

1. Read and study the activity, using the provided references for further research.
2. 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 one of the following statements is true about pneumococcal conjugate vaccines?

   A. Can be used in combination with pneumococcal polysaccharide vaccine.

   B. Contraindicated for patients with egg allergy.

   C. Use of pneumococcal conjugate vaccines has increased invasive pneumococcal disease secondary to vaccine serotypes.

   D. Contraindicated for adults over age 65

2. Pediatric travelers, especially those traveling to visit friends and relatives:

   A. are more likely to have serious travel-related illness than tourist travelers.

   B. are at low risk of getting diarrhea illnesses.

   C. usually obtain good pre-travel consultation.

   D. should be advised not to travel to sub-Saharan Africa.

3. Animal bites in travellers:

   A. Usually result in timely and appropriate initiation of PEP after returning to the home country.

   B. Frequently lead to delay in HRIG even when rabies vaccination may be started at the country of exposure.

   C. Should necessitate serologic testing with rapid focus fluorescent inhibition test immediately.

   D. Most commonly are caused by monkeys and cats.

PHARMACOLOGY WATCH

Supplement to *Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Hospital Medicine Alert, Infectious Disease Alert, Internal Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports, Travel Medicine Advisor.*

Statins and Cognition — More to the Story?

In this issue: Side effects of statins; effects of cannabis use; antihypertensives and lip cancer; and FDA actions.

Review challenges FDA warning

Do statins cause changes in cognition? In February, the FDA added warnings to statin labels regarding the risk of reversible memory loss and confusion. But a new review from the *Journal of the American College of Cardiology* reviews the evidence given to the FDA and concludes "that there is no increased risk of cognitive decline" with statin use. The State-of-the-Art Paper was a comprehensive review of case reports, observational research, and randomized, controlled trials of statins and cognitive change, as well as risk of cancer and diabetes. Most of the evidence for cognitive changes came from individual case reports, many of which were self-reported by consumers to the FDA. Observational studies gave mixed results on cognition with four of nine studies showing statins improved cognition, while three showed no change, and two studies found an increased risk of cognitive impairment. The authors suggest that these studies are inconclusive and prone to selection bias. Two large, randomized, controlled clinical trials specifically looked at the effect of statins on cognitive function as the major secondary endpoint. In both, no significant differences were seen between the study and control groups with regard to cognitive decline. Twelve smaller studies showed mixed results with the majority showing no change and only one in 12 showing a detrimental effect of statins on cognitive function, while two studies showed a benefit. Along with lack of evidence to suggest statins lead to cognitive decline, the authors also found no evidence that statins increase the risk of cancer. They did, however, find a small risk for development of diabetes, which they felt was "outweighed by the cardiovascular benefits in patients for whom statin therapy is recommended" (*J Am Coll Cardiol* published online August 15, 2012). ■

Cannabis use and cognitive decline

Persistent cannabis use — particularly in adolescence — may lead to permanent cognitive decline, according to a new study. Researchers looked at a birth cohort of 1037 healthy individuals in New Zealand who underwent neuropsychological testing in the mid 1980s before the onset of cannabis use, and then again in 2010-2012 after some had developed a persistent pattern of cannabis use. Persistent cannabis use over 20 years (at least 4 days per week) was associated with neuropsychological decline, with greater decline evidence for more persistent users. This effect was only seen in adolescent-onset cannabis users and was associated with an average 8 point loss in IQ by age 38. The effect persisted after controlling for education, other drugs, or tobacco. The effects were not seen among adult-onset cannabis users. The authors conclude that increasing efforts should be directed toward delaying the onset of cannabis use by young people, "particularly given the recent trend of younger ages of cannabis use initiation in the United States and

This supplement was written by William T. Elliott, MD, FACP, Chair, Formulary Committee, Kaiser Permanente, California Division; Assistant Clinical Professor of Medicine, University of California-San Francisco. In order to reveal any potential bias in this publication, we disclose that Dr. Elliott reports no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study. Questions and comments, call: (404) 262-5404. E-mail: neill.kimball@ahcmedia.com.

evidence that fewer adolescents believe that cannabis use is associated with serious health risk." (*Proc Natl Acad Sci U S A* published online August 27, 2012). This study and others are increasingly important as cannabis, the most widely used illicit drug in the world, is being considered for more medicinal uses as well as legalization. ■

Antihypertensives and lip cancer

Two photosensitizing antihypertensives, hydrochlorothiazide and nifedipine, may increase the risk for lip cancer in non-Hispanic white patients, according to a new study from Kaiser Permanente in California. From a large cohort of patients, 712 were identified with lip cancer along with nearly 23,000 matched controls. At least a 5-year supply of the drug resulted in the following odds ratios for lip cancer (95% confidence intervals) — hydrochlorothiazide 4.22 (2.82-6.31), hydrochlorothiazide-triamterene 2.82 (1.74-4.55), nifedipine 2.50 (1.29-4.84), and lisinopril 1.42 (0.95-2.13). When atenolol was given without other hypertensives, the odds ratio for lip cancer was 0.54 (0.07-4.08). The authors suggest that while antihypertensive therapy outweighs the risk of lip cancer, preventive measures should be taken for those at increased risk because of fair skin and long-term sun exposure (*Arch Intern Med* published online August 06, 2012). ■

FDA actions

The FDA has approved a delayed-release form of prednisone for the treatment of endocrine, inflammatory, and neoplastic conditions. Delayed-release prednisone should be taken once a day with timing to be determined by the disease being treated. For example, 10 p.m. dosing is recommended for rheumatoid arthritis, as it is more effective than immediate-release prednisone taken in the morning for treating morning stiffness associated with the disease. Dosing is based on the theory that both cytokines and endogenous cortisol follow a circadian rhythm, and that dosing the drug based on the condition being treated may afford more effective treatment than immediate-release prednisone. The new product delays the release of prednisone by approximately 4 hours. Side effects are the same as short-acting prednisone. Delayed-release prednisone will be marketed as RAYOS by Horizon Pharma.

The FDA has approved a new chlorofluorocarbon (CFC)-free, over-the-counter inhaled racepinephrine product for the treatment of asthma. The new product takes the place of the banned Primatene Mist, which was taken off the market at the end of 2011 because it contained CFCs. Inhaled epinephrine has been used for the treatment of asthma for more than 100 years. Marketed as Asthmanefrin, the new product will be sold as a starter kit and refill package. The starter kit will include 10 vials of racepinephrine along with the EZ Breathe Atomizer. The refill kit will include 30 vials of the drug. The drug is not without controversy, however, with many asthma experts feeling that the side effects of epinephrine are serious and well-documented, and over-the-counter use goes against published guidelines for treating asthma. Asthmanefrin will be marketed by Nephron Pharmaceuticals.

The FDA has approved linaclotide for the treatment of chronic idiopathic constipation and irritable bowel syndrome with constipation. The drug is the first guanylate cyclase (GC-C) agonist that acts locally in the gut with minimal systemic exposure. The drug is taken once daily on an empty stomach at least 30 minutes before the first meal of the day. Safety and efficacy in the management of irritable bowel syndrome with constipation was established in two double-blind studies of nearly 1300 patients who were randomly assigned to linaclotide or placebo for 12 weeks. Patients taking the drug experienced more complete spontaneous bowel movements than those taking placebo. The drug should not be used in patients 17 years or younger. Linaclotide will be jointly marketed by Ironwood Pharmaceuticals and Forest Pharmaceuticals as Linzess.

Montelukast (Singulair), Merck's popular asthma and allergy medication, will soon be available as a generic. The leukotriene receptor antagonist will be manufactured by 10 generic companies in tablet form, oral granules, and chewable tablets. The FDA warns that montelukast should not be used for relief of sudden asthma attacks and further warns that patients should contact a clinic immediately if they are experiencing behavior and mood-related changes such as aggression, depression, or hallucinations.

The FDA has approved the first generic version of pioglitazone (Actos). The drug is approved along with diet and exercise to improve blood sugar control in adults with type 2 diabetes. This happens as thiazolidinediones have generally fallen out of favor for use in type 2 diabetes due to side effects including worsening heart failure and edema. The FDA also recently issued a warning for pioglitazone regarding increased risk of bladder cancer if the drug is taken for more than 1 year. The first generic pioglitazone will be manufactured by Mylan Pharmaceuticals. ■