Medical News

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Update on Malaria Prevention in Travelers

Each year, 25 to 30 million people from nontropical countries visit malaria-endemic countries, and up to 30,000 North American and European travelers contract malaria annually. The evolving patterns of drug resistance among malaria parasites and changes in recommendations for malaria prevention present a challenge to physicians who advise travelers on chemoprophylaxis. Dr. Hans Lobel, of the CDC's Division of Parasitic Diseases, and Dr. Phyllis Kozarsky recently reviewed the strategies to prevent malaria, approaches to avoid human-mosquito contact, and currently recommended drugs for prophylaxis.

Because malaria transmission occurs primarily between dusk and dawn, due to the nocturnal feeding habits of the Anopheles mosquitoes that transmit malaria, reducing risk of contact can be achieved by both remaining in air-conditioned or well-screened rooms and using aerosol insecticides in rooms where mosquitoes are found. Use of mosquito nets impregnated with permethrin and application of insect repellent formulations containing less than 30% DEET (N,N-diethyl-m-toluamide) to exposed skin can reduce risk of mosquito bites further.

Chloroquine-resistant *Plasmodium falciparum* malaria, which emerged in the 1960s, has spread to almost all malaria-endemic countries except Haiti, the Dominican Republic, Central America west of Panama Canal, and parts of the Middle East. In addition to chloroquine resistance, there is a growing problem of resistance of *Plasmodium falciparum* to a combination product of pyrimethamine and sulfadoxine in Southeast Asia, Africa, and the Amazon region. Chloroquine-resistant *Plasmodium vivas* has been identified in Indonesia, Papua New Guinea, Solomon Islands, and Mynmar.

Mefloquine is the drug of choice for chemoprophylaxis for most travelers, with doxycycline and chloroquine being less effective alternatives. Mefloquine is tolerated well at prophylactic dosages, but anecdotal reports have raised concern about its adverse effects. Resistance to this drug has emerged in parts of Southeast Asia and may spread to other parts of the world. The major disadvantages of doxycycline are the need for daily dosing, its contraindication for young children and pregnant women, and its adverse effects. Chloroquine is effective for prophylaxis only in Central America, the Caribbean, and parts of the Middle East.

The authors warn that few new drugs will be available in the near future because of reduced funding for antimalarial drug research and development; therefore, the usefulness of currently available drugs needs to be prolonged by rational use.

FROM: Lobel HO, Kozarsky PE. Update on prevention of malaria in travelers. *JAMA* 1997;278:1767-1771.

Adverse Drug Events Are Costly

The annual national cost of drug-related morbidity and mortality has been estimated at more than $136 billion. Because of the current economic crisis within hospitals, quality-improvement efforts that are cost-effective are likely to be pursued. Moreover, despite the widespread impression that adverse drug events (ADEs) in hospitals are costly, few data are available to quantify the additional resource utilization associated with these events. Two recent studies examined the costs associated with ADEs.

Boston researchers from Brigham and Women's Hospital, Harvard Medical School, and the West Roxbury Veterans' Administration Medical Center recently reported the results of a prospective cohort study to define the costs associated with ADEs. The cohort included 4,108 admissions to a stratified random sample of 11 medical and surgical units in two tertiary-care hospitals over a 6-month period. Incidents were detected by self-report and daily chart review, and were classified as to whether they represented ADEs.[1]

The primary outcome of this study was the ADE, defined as an injury resulting from medical intervention related to a drug. An example given was a patient who received a beta blocker and developed complete heart block requiring temporary pacing. If the patient had been taking channel blocker already and had first-degree atrioventricular block, the event would be considered a preventable ADE. Potential ADEs, in which an error was made but no harm occurred, were not included in the study.

During the study there were 247 ADEs among 207 admissions. After outliers and multiple episodes were excluded, there were 190 ADEs, of which 60 were preventable. In a paired regression analysis adjusting for multiple factors, including severity, comorbidity, and case mix, the additional length of stay associated with an ADE was 2.2 days, and the increased cost associated with an ADE was $3,244. For preventable ADEs, the increases were 4.6 days in length of stay and $5,857 in total cost. Based on these costs and data on the incidence of ADEs, the researchers estimated that annual costs attributable to all ADEs and preventable ADEs for a 700-bed teaching hospital are $5.6 million and $2.8 million, respectively. They pointed out that these estimates were conservative, because they did not include the costs of the injuries to patients or malpractice costs.

In a second study, researchers from the LDS Hospital

https://doi.org/10.1017/S019594170008721X Published online by Cambridge University Press

in Salt Lake City, Utah, conducted a matched case-control study with 1,580 cases and 20,197 controls.[2] ADEs were found to complicate 2.43 per 100 admissions to the LDS Hospital during the 4-year study period from January 1, 1990, to December 31, 1993. The crude mortality rates for cases and matched controls were 3.5% and 1.05%, respectively. The mean length of stay significantly differed between the cases and matched controls (7.69 days vs 4.46 days), as did the mean cost of hospitalization ($10,010 vs $5,355) The extra length of hospital stay attributable to an ADE was $2,013.

Both studies confirm that substantial costs of ADEs justify investment in effort to prevent these events.

FROM: 1. Bates DW, Spell N, Cullen DJ, Burdick E, Laird N, Peterson LA.. The cost of adverse drug events in hospitalized patients. *JAMA* 1997;277:307-311.

2. Classen DC, Pestonik SL, Evans RS, Lloyd JF, Burke JP. Adverse drug events in hospitalized patients. *JAMA* 1997;277:301-306.

CDC's Immunization Practices Advisory Committee Revises Childhood Immunization Schedule

The CDC's Immunization Practices Advisory Committee, the American Academy of Pediatrics, and the American Academy of Family Physicians recently changed some recommendations for childhood vaccination.

Poliovirus vaccines. The recommended age has been changed for administration of the third dose of inactivated poliovirus vaccine (IPV) in an all-IPV schedule to 6 to 18 months. The recommended ages for administration of polio vaccine in either an all-oral poliovirus vaccine or an all-IPV schedule are now the same (2, 4, 6-18 months, and 4-6 years).

Measles-mumps-rubella. The recommended age for the second dose of measles-mumps-rubella vaccine is now 4 to 6 years.

Hib Vaccines. Three *Haemophilus influenzae* type b (Hib) vaccines are licensed for infant immunization: (1) oligosaccharide conjugate Hib vaccine HibTITER (Wyeth-Lederle Laboratories, Pearl River, NY), (2) polyribosylribitol phosphate-tetanus toxoid conjugate (ActHIB and Omni-HIB, manufactured by Pasteur Merieux Connaught, Lyon, France, and distributed by Pasteur Merieux Connaught–USA, Swiftwater, PA, and SmithKline Beecham Pharmaceuticals, Philadelphia, PA), and (3) *Haemophilus* b conjugate vaccine (meningococcal protein conjugate; PRP-OMP; PedvaxHIB, Merck, Inc, West Point, PA). These products now are considered interchangeable for primary, as well as booster, vaccination. If PRP-OMP is administered in a series with one of the other two products licensed for infants, the recommended number of doses to complete the series is determined by the other product (and not by the PRP-OMP). For example, if PRP-OMP is administered for the first dose at age 2 months and another vaccine is administered at age 4 months, a third dose of any of the three licensed Hib vaccines is recommended at age 6 months to complete the primary vaccine series.

Hepatitis B vaccine. For children born to hepatitis B surface antigen-negative mothers, the third dose of HBV should be administered at least 2 months after the second dose, but not before age 6 months. This represents a clarification in wording of the recommendations.

Other vaccines. The routine visit to the healthcare provider for adolescents aged 11 to 12 years remains an important time to ensure receipt of two doses of measles-mumps-rubella vaccine beginning at or after age 12-months, one dose of varicella vaccine, and initiation or completion of the HBV vaccine series. Diphtheria and tetanus toxoid boosters still need to be administered routinely to all children at this age.

FROM: Centers for Disease Control and Prevention. Recommended childhood immunization schedule, United States, 1998. *MMWR* 1998;47(1):8-12.

Guidelines for Antiretrovirals in Pediatric HIV

The US Health Resources and Services Administration recently announced the availability of "Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection." This document may be obtained from the National AIDS Clearinghouse at 1-800-458-5231, or at http://www.cdcnac.org, or from the HIV/AIDS Treatment Information Service at 800-448-0440 or http://www.hivatis.org.

Typing of *Nocardia farcinica*

German investigators from the Institute for Medicine, Microbiology, and Immunology at the University of Bonn conducted a study on severe postoperative wound infections caused by *Nocardia farcinica,* observed repeatedly in a German hospital surgical ward. A pulsed-field gel electrophoresis protocol was established to characterize the genetic relatedness of the bacterial isolates from these infections. All 18 isolates from postoperative infections that have occurred since 1985 belong to a common endemic genotype; organisms of this genotype also were detected in the air of two rooms of the department where these postoperative infections occurred. In contrast, two environmental isolates from another building on the same campus showed a distinct genotype. Three cases of pulmonary infections, at a department that is located in proximity to the surgical department, also were caused by the endemic type, which suggests aerogenic spread of the endemic strain to these patients. Controls consisting of epidemiologically unrelated isolates from sporadic infections in other towns belonged in each case to a different genotype. Pulsed-field gel electrophoresis was shown to be suited well to differentiate various types of *N farcinica* and revealed an endemic strain causing postoperative wound infections possibly after aerogenic transmission.

FROM: Blumel J, Blumel E, Yassin AF, Schmidt-Rotte H, Schaal KP. Typing of *Nocardia farcinica* by pulsed-field gel electrophoresis reveals an endemic strain as source of hospital infections. *J Clin Microbiol* 1998;36:118-122.

https://doi.org/10.1017/S019594170008721X Published online by Cambridge University Press