

Fast Track Vaccinations for Young Globetrotters

BY JANE SALODOF MACNEIL
Southwest Bureau

ASPEN, COLO. — Routine vaccinations can be accelerated to protect very young travelers against infectious diseases in developing countries, Sarah K. Parker, M.D., advised at a conference on pediatric infectious diseases sponsored by Children's Hospital, Denver.

"They can be really protected by about 13½ months of age," said Dr. Parker of

Children's Hospital and a faculty member in pediatric infectious diseases at the University of Colorado Health Sciences Center, Denver.

Dr. Parker also recommended that physicians do a pretravel assessment to identify additional vaccination requirements by endemic conditions in destination countries. The assessment would include consideration of chemoprophylaxis and counseling parents on ways to prevent infectious disease while traveling abroad.

"Infection only causes about 1% of traveler deaths. However, it is a large fraction of what causes illness while traveling," she said. About 50%-70% of travelers become ill. About 40% of illnesses are diarrhea, which can be more severe and more prolonged in children.

Routine vaccinations can start at 6 weeks of age, she said, outlining an accelerated schedule. Babies can receive four doses of inactivated polio vaccine; three doses of DTaP vaccine, *Haemophilus influenzae* type b vaccine, and seven-valent pneumococcal polysaccharide vaccine; and two doses of hepatitis B virus vaccine by 14 weeks.

MMR can be given at 6 months, she said, but does not count. If given at 12 months, it can be followed by a booster at 13 months. The accelerated schedule also permits hepatitis A virus vaccine off-label at 12 months.

A family traveling to Africa's "meningitis belt" should use the polysaccharide conjugate vaccine for children older than 11 years, the polysaccharide meningococcal vaccine for children 2-11 years, and consider its use off label in younger children at high risk, she said. The polysaccharide vaccine has been studied at 3 months with a 12-month booster with a rise in titers against meningococcus A, the predominant strain in Africa.

Varicella zoster virus (VZV) and influenza vaccines cannot be accelerated, however.

If one is protecting against hepatitis A with hepatitis A immunoglobulin, Dr. Parker noted that hepatitis A IgG interferes with MMR and VZV. Therefore, MMR and/or VZV vaccines should be given 2 weeks earlier, she said, adding that hepatitis A vaccine and IgG can be given together. Hepatitis A IgG must be repeated every 5 months while the child is in an endemic area.

Dr. Parker urged primary care physicians to consider prevalence of disease in destination nations when reviewing itineraries. Influenza should not be overlooked, she said. It is endemic year-round close to the equator and from March to October in the southern hemisphere. She suggested stockpiling flu vaccine released in October for use through June 30.

Meningococcal vaccine is required for pilgrims making the hajj, Dr. Parker noted. She said it also should be considered, even if off label, for children heading to Africa's "meningitis belt" and other potential risk areas.

Causing 22 million cases a year, *Salmonella typhi* is a concern throughout the developing world, she said. She advised vaccinating anyone older than 2 years of age who is heading to an endemic area.

Two vaccines are options if typhoid is a risk, Dr. Parker said. The injectable capsular polysaccharide vaccine is approved for children over 2 years and can be given 2 weeks prior to travel. Oral live, attenuated Ty21 a virus vaccine is approved for children older than 6 years but cannot be given if the child is immunodeficient.

Yellow fever vaccine is indicated for travel to endemic areas and required by some countries unless contraindicated. It should not be given to infants younger than 4 months old and is contraindicated in infants 5-9 months of age. Because encephalitis can be a side effect, "you don't want to give it to someone who doesn't need it," she advised.

Japanese encephalitis is a risk in parts of Asia. Mortality is high, however, with deaths in 5%-30% of those who develop symptoms, according to Dr. Parker.

If mosquito exposure is likely during an extended stay in an endemic area during the endemic season, she recommended vaccination with an inactivated virus. It is approved for persons over 1 year of age. Because severe allergic reactions can occur up to 10 days afterward, she said this vaccine should be given at least 2 weeks in advance of travel.

No drug can prevent malarial infection, Dr. Parker said, but some agents can prevent disease. For pediatric considerations in prophylaxis, she referred physicians to a journal article (Semin. Pediatr. Infect. Dis. 2004;15:137-49).

Whether or not prophylaxis is used, families should try to prevent mosquito bites by making careful use of *N,N*-diethyl-m-toluamide (DEET), wearing permethrin-treated clothing, and covering exposed skin.

Dogs and sweets pose special risks when traveling with young children who love

Some Travel Health Web Sites

CDC Traveler's Health Web Site
www.cdc.gov/travel/destinat.htm

CDC Yellow Book
<http://www.cdc.gov/travel/yb/index.htm>

World Health Organization Vaccine Preventable Diseases Monitoring System
(Vaccine schedules listed by country)
www.who.int/immunization_monitoring/en/globalsummary/scheduleselect.cfm

WHO Global Health Atlas
(Communicable disease, including rabies)
www.who.int/globalatlas

Pan American Health Organization
www.paho.org

International Association for Medical Assistance to Travelers (IAMAT)
www.iamat.org

U.S. State Department
http://travel.state.gov/travel/travel_1744.html

Source: Dr. Parker

both. Along with the usual dietary precautions, Dr. Parker warned that frozen desserts may not be pasteurized. Parents should be told to seek care early if a child gets diarrhea. Much of the world has dog rabies, she added, so teaching children not to pet animals is important, albeit difficult. She recommended vaccinating children against rabies before travel to highly endemic areas. But she warned that a vaccinated child would have to be revaccinated if bitten.

"Vaccination is not enough. It just buys time," Dr. Parker said, noting that post-exposure prophylaxis is not available in some countries. ■

Visits to Families Abroad Pose Risks

Foreign-born families taking young children to meet relatives in their home countries face significantly greater health risks, compared with other travelers, according to Dr. Parker.

The youngsters are often very young; mothers may travel while pregnant; and, sometimes, family members are ill even before they leave on trips timed to family occasions, she said.

These families also stay longer, use less safe local transportation, and have difficulty refusing unsafe food or water in the homes of friends and relatives, Dr. Parker observed. As a result, visitors of friends and relatives are 10 times as likely to get malaria or typhoid as tourists.

Yet, foreign-born parents often do not seek medical advice before these journeys, according to Dr. Parker. Even if they have concerns, many don't seek pretravel advice because of the expense.

Some do not believe their families have to worry about organisms in the communities where they grew up. These travelers often see themselves and their children as "already immune," which in large part is a myth, especially for their children, she said.

Even if they see a physician, travelers going back home are less likely to follow medical advice than are ecotourists, adventurers, missionaries, or relief workers traveling to developing countries.

VYTORIN® (ezetimibe/simvastatin)

VYTORIN: There are insufficient data for the safe and effective use of VYTORIN in pediatric patients. (See *Ezetimibe* and *Simvastatin* below.)

Ezetimibe: The pharmacokinetics of ezetimibe in adolescents (10 to 18 years) have been shown to be similar to that in adults. Treatment experience with ezetimibe in the pediatric population is limited to 4 patients (9 to 17 years) with homozygous sitosterolemia and 5 patients (11 to 17 years) with HoFH. Treatment with ezetimibe in children (<10 years) is not recommended.

Simvastatin: Safety and effectiveness of simvastatin in patients 10-17 years of age with heterozygous familial hypercholesterolemia have been evaluated in a controlled clinical trial in adolescent boys and in girls who were at least 1 year post-menarche. Patients treated with simvastatin had an adverse experience profile generally similar to that of patients treated with placebo. **Doses >40 mg have not been studied in this population.** In this limited controlled study, there was no detectable effect on growth or sexual maturation in the adolescent boys or girls, or any effect on menstrual cycle length in girls. Adolescent females should be counseled on appropriate contraceptive methods while on therapy with simvastatin (see CONTRAINDICATIONS and PRECAUTIONS, *Pregnancy*). Simvastatin has not been studied in patients younger than 10 years of age, nor in pre-menarchal girls.

Geriatric Use

Of the patients who received VYTORIN in clinical studies, 792 were 65 and older (this included 176 who were 75 and older). The safety of VYTORIN was similar between these patients and younger patients. Greater sensitivity of some older individuals cannot be ruled out. (See CLINICAL PHARMACOLOGY, *Special Populations* and ADVERSE REACTIONS.)

ADVERSE REACTIONS

VYTORIN has been evaluated for safety in more than 3800 patients in clinical trials. VYTORIN was generally well tolerated.

Table 1 summarizes the frequency of clinical adverse experiences reported in ≥2% of patients treated with VYTORIN (n=1236) and at an incidence greater than placebo regardless of causality assessment from 3 similarly designed, placebo-controlled trials.

Table 1*
Clinical Adverse Events Occurring in ≥2% of Patients Treated with VYTORIN and at an Incidence Greater than Placebo, Regardless of Causality

Body System/ Organ Class Adverse Event	Placebo (%) n=311	Ezetimibe 10 mg (%) n=302	Simvastatin** (%) n=1234	VYTORIN** (%) n=1236
Body as a whole - general disorders				
Headache	6.4	6.0	5.9	6.8
Infection and infestations				
Influenza	1.0	1.0	1.9	2.6
Upper respiratory tract infection	2.6	5.0	5.0	3.9
Musculoskeletal and connective tissue disorders				
Myalgia	2.9	2.5	2.6	3.5
Pain in extremity	1.3	3.0	2.0	2.5

* Includes 2 placebo-controlled combination studies in which the active ingredients equivalent to VYTORIN were coadministered and 1 placebo-controlled study in which VYTORIN was administered.

** All doses.

Post-marketing Experience: The adverse reactions reported for VYTORIN are consistent with those previously reported with ezetimibe and/or simvastatin.

Ezetimibe: Other adverse experiences reported with ezetimibe in placebo-controlled studies, regardless of causality assessment: *Body as a whole - general disorders*: fatigue; *Gastrointestinal system disorders*: abdominal pain, diarrhea; *Infection and infestations*: infection viral, pharyngitis, sinusitis; *Musculoskeletal system disorders*: arthralgia, back pain; *Respiratory system disorders*: coughing.

Post-marketing Experience: The following adverse reactions have been reported in post-marketing experience, regardless of causality assessment: Hypersensitivity reactions, including angioedema and rash; elevated creatine phosphokinase; elevations in liver transaminases; hepatitis; thrombocytopenia; pancreatitis; nausea; cholelithiasis; cholecystitis; and, very rarely, myopathy/rhabdomyolysis (see WARNINGS, *Myopathy/Rhabdomyolysis*).

Simvastatin: Other adverse experiences reported with simvastatin in placebo-controlled clinical studies, regardless of causality assessment: *Body as a whole - general disorders*: asthenia; *Eye disorders*: cataract; *Gastrointestinal system disorders*: abdominal pain, constipation, diarrhea, dyspepsia, flatulence, nausea; *Skin and subcutaneous tissue disorders*: eczema, pruritus, rash.

The following effects have been reported with other HMG-CoA reductase inhibitors. Not all the effects listed below have necessarily been associated with simvastatin therapy. *Musculoskeletal system disorders*: muscle cramps, myalgia, myopathy, rhabdomyolysis, arthralgias.

Nervous system disorders: dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, dizziness, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy, psychic disturbances.

Ear and labyrinth disorders: vertigo.

Psychiatric disorders: anxiety, insomnia, depression, loss of libido.

Hypersensitivity Reactions: An apparent hypersensitivity syndrome has been reported rarely which has included 1 or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, dermatomyositis, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, eosinophilia, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

Gastrointestinal system disorders: pancreatitis, vomiting.

Hepatobiliary disorders: hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma.

Metabolism and nutrition disorders: anorexia.

Skin and subcutaneous tissue disorders: alopecia, pruritus. A variety of skin changes (eg, nodules, discoloration, dryness of skin/mucous membranes, changes to hair/nails) have been reported.

Reproductive system and breast disorders: gynecomastia, erectile dysfunction.

Eye disorders: progression of cataracts (lens opacities), ophthalmoplegia.

Laboratory Abnormalities: elevated transaminases, alkaline phosphatase, γ-glutamyl transpeptidase, and bilirubin; thyroid function abnormalities.

Laboratory Tests

Marked persistent increases of serum transaminases have been noted (see WARNINGS, *Liver Enzymes*). About 5% of patients taking simvastatin had elevations of CK levels of 3 or more times the normal value on 1 or more occasions. This was attributable to the noncardiac fraction of CK. Muscle pain or dysfunction usually was not reported (see WARNINGS, *Myopathy/Rhabdomyolysis*).

Concomitant Lipid-Lowering Therapy

In controlled clinical studies in which simvastatin was administered concomitantly with cholestyramine, no adverse reactions peculiar to this concomitant treatment were observed. The adverse reactions that occurred were limited to those reported previously with simvastatin or cholestyramine.

Adolescent Patients (ages 10-17 years)

In a 48-week controlled study in adolescent boys and girls who were at least 1 year post-menarche, 10-17 years of age with heterozygous familial hypercholesterolemia (n=175), the safety and tolerability profile of the group treated with simvastatin (10-40 mg daily) was generally similar to that of the group treated with placebo, with the most common adverse experiences observed in both groups being upper respiratory infection, headache, abdominal pain, and nausea (see CLINICAL PHARMACOLOGY, *Special Populations* and PRECAUTIONS, *Pediatric Use*).



MERCK / Schering-Plough Pharmaceuticals

Manufactured for: MERCK/Schering-Plough Pharmaceuticals
North Wales, PA 19454, USA

©Merck/Schering-Plough Pharmaceuticals, 2005.

All rights reserved. 20506478(1)(603)-VYT