

Home-Use Antibacterials: High Risk, Low Benefit

An FDA panel found antibacterial detergents and soaps ineffective and environmentally unsound.

BY MARK S. LESNEY
Senior Editor

SILVER SPRING, MD. — Several decades' worth of clinical data on antibacterial additives in home-use soaps and detergents has shown no benefit over plain soap and water in reducing infection, the Food and Drug Administration's advisory panel on nonprescription drugs found at its recent meeting.

Lacking such clear benefits, compounds such as triclosan and triclocarban pose unacceptable risks of environmental contamination and contribution to the evolution of antibiotic resistance, the panel unanimously concluded.

Evidence on the efficacy of alcohol-based gels and wipes was found to be similar (no more effective in reducing infection than soap and water). However, their utility in situations where water was not available, safe, or convenient—combined with their low risk of contributing to the development of resistant bacteria—was recognized by the panel, which recommended the products' continued use in defined circumstances.

A 1994 FDA decision said that antibacterial consumer products were deemed effective if they could meet the surrogate end point of decreasing bacterial load on the skin. Such a decrease was assumed to be clinically significant, according to the 1994 monograph.

However, subsequent, real-world clinical

trials, though imperfect in design, have been unable to demonstrate a corresponding decrease in disease incidence or severity, compared with soap and water, either for respiratory or GI infections.

It was this question of efficacy of consumer antiseptic products that the FDA asked its advisory panel to address.

The panel heard presentations of clinical evidence regarding the benefits of consumer antiseptics from Steven Osborne, M.D., medical officer at FDA's Office of Nonprescription Products, and Allison E. Aiello, Ph.D., of the University of Michigan School of Public Health, Ann Arbor.

In eight studies from the literature, use of plain or unidentified soap and water reduced cases of diarrhea from 30% to 89% (median reduction 53%). In three studies comparing antiseptic soap with no soap in control groups, reductions in diarrhea with antiseptic soap ranged from 29% to 50%.

Furthermore, five studies comparing antiseptic soaps with plain soap found no statistically significant difference for all infectious symptoms, the presenters said.

Stuart B. Levy, M.D., a professor at Tufts University, Boston, spoke on the products' contribution to bacterial resistance.

"What are we worried about?" he asked, "We are worried that an antibiotic can select this kind of mutant and make it resistant to biocides . . . Or we could be using the biocides and select a mutant which now is resistant to antibiotics. We're not talking about just one [antibiotic]. We're

talking about tetracycline, penicillin, fluoroquinolone, chloramphenicol."

Such resistance can also develop to the biocides themselves, he added. "I'm not saying I don't see the need for biocides—I don't see that they are needed in consumer products."

The impact of triclosan and triclocarban accumulation in the environment was discussed by Rolf U. Halden, Ph.D., of Johns Hopkins University, Baltimore.

In samples of surface water from the Baltimore area, Dr. Halden and colleagues found triclocarban concentrations of 6,750 ng/L (*Environ. Sci. Technol.* 2005;39:1420-6). According to Dr. Halden, his results suggest triclocarban is a previously unrecognized contaminant of U.S. water resources nationwide, probably in the top 10 in occurrence rates and in the top 20 in maximum concentration.

The amount of triclocarban contamination was markedly higher than the non-peer-reviewed numbers (240 ng/L) used by the Environmental Protection Agency to evaluate ecological and human health risks, he said. The predicted half-life of triclocarban ranged from less than a day in air to 540 days in sediment. Cooccurrence of triclosan was observed at all sites.

Dr. Halden questioned why manufacturers were still using vast quantities of chlorinated compounds that could migrate into the environment, given the dubious nature of chlorine chemistry in the previous history of pollutants.

Several presenters highlighted the importance of hand hygiene in preventing the transmission of infectious diseases and the effectiveness of antibacterial products

in reducing or eliminating bacteria from the skin.

"Every 3 minutes, a child brings his/her hand to nose or mouth. Every 60 seconds, a working adult touches as many as 30 objects," said Charles P. Gerba, Ph.D., of the University of Arizona, Tucson. "Washing fomites with soap and water is not enough to prevent the spread of pathogens."

Targeted hygiene by handwashing after risk exposure (bathrooms, food preparation, contact with potentially infected people) is needed for home infection control, he said, adding that the data clearly show that antiseptic products "decrease bacteria on the skin" and follow the log reduction requirements after a single wash.

The utility of antibacterial consumer products was stressed by the Cosmetic, Toiletry, and Fragrance Association (CTFA), which said "the benefits of topical OTC antimicrobial drug products clearly support the current proposed labeling indication (i.e., 'to decrease bacteria on skin') and provide consumers an effective means of controlling the risks of infection."

CTFA had previously asked the FDA to lower the threshold for approval of consumer antibacterial products. That request was not recommended by the panel at a meeting in March 2005. At that meeting, the panel voted unanimously to recommend retention of the standards for bacteria reduction in antibacterial and antiseptic products for nonconsumer products.

The FDA usually follows the recommendations of its advisory panels but is not obligated to do so.

Final review of these products is to be concluded by 2007. ■

Five Unvaccinated Amish Children Positive for Poliovirus in Minnesota

BY ROBERT FINN
San Francisco Bureau

A small outbreak of poliovirus infection has been reported among unvaccinated children living in rural Minnesota. All cases to date have been linked to the live attenuated virus used in the oral polio vaccine, according to the Minnesota Department of Health and the Centers for Disease Control and Prevention.

Because oral polio vaccine (OPV) is known to cause paralysis in about 1 in every 13 million doses, its use was discontinued in Canada in 1997 and in the United States in 2000. An injected inactivated polio vaccine (IPV) is used instead in accordance with recommendations by the CDC's Advisory Committee on Immunization Practices and the American Academy of Pediatrics Committee on Infectious Diseases. But other countries around the world continue to use OPV. Health workers presume that a person vaccinated

with OPV in another country was the original source of the outbreak, according to the CDC report.

The five Minnesota children reported to have poliovirus infection are members of a remote Amish community in central Minnesota. The Amish often decline to vaccinate their children. None of the children exhibited the flaccid paralysis that accompanies poliovirus infection in 1 of every 200 cases. The first four cases are described by the CDC (*MMWR* 2005;54:1053-5) and the fifth case was reported at press time.

The polio outbreak was discovered by chance on Sept. 29, 2005, during testing of a stool sample from a 7-month-old infant with severe combined immunodeficiency disease. Subsequent testing of other community members uncovered infections from the same viral strain in three unvaccinated siblings from an unrelated family, and a fifth unvaccinated child from a third family. All three families are members of the same small Amish

community, which includes about 200 members in 24 families.

Partial sequencing of the viral capsid identified it as a type 1 poliovirus derived from one of the three strains in the Sabin oral poliovirus vaccine (OPV). The viral sequence differed from the original vaccine strain by 2.3%. This vaccine is known to mutate at a rate of about 1% per year, suggesting that it's been circulating for 2-3 years.

Although the source of the infection likely was someone who received OPV abroad, none of the infected children or their family members had a recent history of international travel or contact with foreigners, and the central Minnesota Amish community in which the infections occurred has little association with outsiders.

Public health officials have been going door to door in the affected community offering vaccinations. IPV offers protection against the OPV-derived vaccine strain of polio. ■

Tick-Borne Lyme Pathogen Tied to Cutaneous Lymphoma

LONDON — *Borrelia burgdorferi* from tick bites, the causative agent of Lyme disease in the United States, has been linked to cases of primary cutaneous B-cell lymphoma in certain areas of Europe, reported Rein Willemze, M.D.

"It is common dermatologic knowledge in Europe that *B. burgdorferi* infections can cause reactive B-cell proliferations in the skin," Dr. Willemze said at the 14th Congress of the European Academy of Dermatology and Venereology. The lesions typically are located on the ear lobes and nipples, which are sites that attract ticks, and most often are marginal zone lymphomas.

Primary cutaneous marginal zone B-cell lymphomas are low-grade malignancies characterized by clonal proliferation of small neoplastic B cells with a Bcl-2+, Bcl-6-, CD10- phenotype, said Dr. Willemze of Leiden (the Netherlands) University Medical Center.

B. burgdorferi-associated cutaneous lymphomas have been reported in Austria and Scotland, though not in Asia or North America. "The most likely explanation is that different subspecies of *B. burgdorferi* are present in these parts of the world," he said.

Systemic antibiotics, usually penicillin, cephalosporins, or tetracyclines, may be curative if lymphoma is associated with *Borrelia* infection, although the optimal regimen has not been established, said Dr. Willemze, who is in the Dutch Cutaneous Lymphoma Working Group.

The relationship between low-grade B-cell lymphomas and bacterial infections is not restricted to the skin. More recognized is the relationship between gastric mucosa-associated lymphoid tissue (MALT) lymphomas, which are similar to primary cutaneous B-cell lymphomas in the skin, and *Helicobacter pylori* infections.

—Nancy Walsh