

**TAB 8 Recommendations of the Council on Scientific Affairs for
the American Medical Association on Consumer Antiseptic
Products**

**Tan, L, Nielsen, NH, Young, DC, and Trizna, Z. Use of antimicrobial
agents in consumer products. *Arch Dermatol.* 2002; 138:1082-1086.**

Use of Antimicrobial Agents in Consumer Products

Litjen Tan, PhD; Nancy H. Nielsen, MD, PhD; Donald C. Young, MD; Zoltan Trizna, MD, PhD;
for the Council on Scientific Affairs, American Medical Association

Objectives: To summarize available data on the effectiveness of antimicrobial ingredients in consumer products such as hand lotions and soaps and to discuss the implications of such use on antimicrobial resistance.

Data Sources: We searched the MEDLINE database, 1966 to 2001, using the search term *resistance* qualified with the terms *consumer product(s)*, OR *soap*, OR *lotion*, OR *triclosan*, and LexisNexis and the World Wide Web using the search strategy *antimicrobial resistance AND consumer product*.

Data Extraction: English-language articles were selected that provided information on the use of antimicrobial ingredients in consumer products and the effect of this use on antimicrobial resistance.

Data Synthesis: Despite the recent substantial increase in the use of antimicrobial ingredients in consumer products, the effects of this practice have not been studied extensively. No data support the efficacy

or necessity of antimicrobial agents in such products, and a growing number of studies suggest increasing acquired bacterial resistance to them. Studies also suggest that acquired resistance to the antimicrobial agents used in consumer products may predispose bacteria to resistance against therapeutic antibiotics, but further research is needed. Considering available data and the critical nature of the antibiotic-resistance problem, it is prudent to avoid the use of antimicrobial agents in consumer products.

Conclusions: The use of common antimicrobials for which acquired bacterial resistance has been demonstrated should be discontinued in consumer products unless data emerge to conclusively show that such resistance has no effect on public health and that such products are effective at preventing infection. Ultimately, antibiotic resistance must be controlled through judicious use of antibiotics by health care professionals and the public.

Arch Dermatol. 2002;138:1082-1086

ANTIMICROBIAL resistance has been a major public health issue for many years, and many aspects of this issue have been addressed in expert reviews and guidelines.¹⁻¹¹ Herein we consider whether the use of antimicrobial agents in consumer products such as antibacterial hand lotions and soaps might be a significant source of antimicrobial resistance with negative implications for public health.

METHODS

We conducted literature searches in the MEDLINE database for articles published between 1966 and 2001 using the search term *resistance* qualified with the terms *consumer product(s)*, OR *soap*, OR *lotion*, OR *triclosan* and found 104 references. Forty-three English-language references contained information relevant to the

use of antimicrobial agents in consumer products and resistance, and these 43 were examined further. Additional references were culled from the bibliographies of these 43 pertinent references. We also searched

For editorial comment see page 1087

LexisNexis news databases and the World Wide Web for current developments using the search strategy *antimicrobial resistance AND consumer product*.

ANTIMICROBIAL INGREDIENTS USED IN CONSUMER PRODUCTS

Many types of antimicrobial ingredients are used in antiseptics (products that prevent infection by inhibiting the growth of infectious agents) and disinfectants (products that prevent infection by destroying or inhibiting the growth or activity of infec-

From the Council on Scientific Affairs, American Medical Association, Chicago, Ill. A complete list of the members and staff of the Council at the time this report was prepared appears on page 1085 of this article.

Antimicrobial Agents Commonly Used as Ingredients in Consumer Products

Product	Applications	Antimicrobial Activity/Mechanism
Anilides, primarily triclocarban	Soap, deodorant	Triclocarban is active against gram-positive bacteria; it demonstrates limited activity against gram-negative bacteria and fungi. ¹² Triclocarban is believed to work by destroying the selectively permeable nature of the bacterial cell membrane, resulting in cell death. ¹²
Bis-phenols, primarily triclosan	Toothpaste, mouthwash, handwash, hand lotion	Triclosan has primary activity against gram-positive bacteria, with less efficacy against gram-negative bacteria and fungi (may be improved by formulation effects). ¹²⁻¹⁴ It exerts antimicrobial effects by inhibiting bacterial fatty acid synthesis at the enoyl-acyl carrier protein reductase step. ^{15,16}
Quaternary ammonium compounds (QACs), primarily cetylpyridium chloride and cetrimide	Disinfectants, antiseptics	QACs are believed to work by disrupting the structural and functional characteristics of the cell membrane ¹² ; for example, cetrimide disrupts the proton motive force of the bacterial cell membrane required for solute transport and generation of adenosine triphosphate at the cell membrane. ¹² These compounds inhibit the growth of bacterial spores by an as yet unknown mechanism.
Biguanides, primarily chlorhexidine	Antiseptic products (eg, mouthwash, handwash)	Chlorhexidine has a broad spectrum of activity and is effective against mycobacteria and nonsporulating bacteria, but it also inhibits spore growth, yeast, and protozoa. ¹⁷ Its broad antimicrobial effect is due to its disruption of the cytoplasmic or inner membrane of the bacteria, resulting in a loss of membrane potential ¹⁸ ; in yeast, it attacks the plasma membrane. ¹²

tious agents on and in any surface). These include the alcohols, aldehydes, biguanides, anilides, halogen-releasing agents, quaternary ammonium compounds (QACs), peroxygens, bis-phenols, and many others.¹² Herein, we focus specifically on the ingredients commonly used in topical, over-the-counter antimicrobial consumer products such as soaps and lotions. These ingredients are primarily anilides (such as triclocarban), bis-phenols¹²⁻¹⁶ (particularly triclosan), QACs (such as cetylpyridium chloride), and to a lesser extent the biguanides^{17,18} (particularly chlorhexidine) (**Table**).¹² These products are to be distinguished from the therapeutic antibiotics, such as the fluoroquinolones and cephalosporins, which are used to treat pathogenic bacterial infections in humans.

BENEFITS OF ANTIMICROBIAL USE IN CONSUMER PRODUCTS

Scientific data are lacking to indicate that use of these antimicrobial ingredients in consumer products such as hand care products, soaps, and food preparation products has any proven infection-prevention benefit.^{19,20} Despite this lack of data, more than 45% of consumer soaps contain an antimicrobial agent.²⁰ In

preparing its position statement on the use of antimicrobial household products, the Association for Professionals in Infection Control and Epidemiology (APIC) performed a systematic search of the current literature and analyzed data provided by as many as 11 companies.²¹ A nonprofit, international organization, APIC is recognized for its leadership in infection control, with more than 110 regional chapters in the United States and more than 12000 members worldwide. The APIC Guidelines Committee concluded that "the literature yielded no scientific data supporting the use of antimicrobial agents in household products as a means to prevent infection."¹⁹ Additionally, the Committee stated that data supplied by manufacturers in response to APIC's request for information did not substantiate product label claims.²¹ The APIC Position Statement on the use of antimicrobial household products concludes that "there is no proven infection benefit in the use of these products. APIC does not advocate the use of antimicrobial household products which are marketed with the implication of preventing infections."¹⁹

However, significant data exist to indicate that use of antimicrobial wash products containing some of the

antimicrobial ingredients described above (eg, triclosan, chlorhexidine) has an important role in preventing nosocomial infections in clinical settings such as hospitals, nursing homes, and neonatal nursery facilities.^{13,14,22-29} These studies suggest that when used properly, these antimicrobial agents significantly decrease the incidence of infection caused by a variety of gram-positive bacteria and, in the case of chlorhexidine, fungi. It is important to note that the patterns of use of these antimicrobial agents in the clinical setting are dramatically different from those in the consumer environment and thus efficacy in the clinical environment will not necessarily translate to efficacy for the consumer.

RESISTANCE TO ANTIMICROBIAL INGREDIENTS USED IN CONSUMER PRODUCTS

Resistance to antimicrobial products can occur via 2 mechanisms. Intrinsic resistance is due to a natural property of the organism and therefore is an innate characteristic of the microbial genome.^{12,30,31} Acquired resistance, which is the form of significant concern, occurs via mutation or by acquisition of a plasmid or transposable element carrying the gene(s)

for resistance. Thus, the natural resistance of gram-negative bacteria to many antimicrobial agents because of the barrier properties of the outer membrane is an example of intrinsic resistance, while the acquisition of multidrug resistance by *Salmonella* is an example of acquired resistance. Since the effect of antimicrobial resistance on public health results primarily from acquired resistance, this report considers only acquired resistance issues with respect to the antimicrobial ingredients used in consumer products.

It is important to note that methods of antimicrobial use differ between consumer and therapeutic applications, and so the therapeutic standard of measuring resistance may be inappropriate for consumer products. Thus, measurement of the minimum inhibitory concentrations is not always appropriate. In fact, while an increase of an antibiotic's minimum inhibitory concentration will have significant therapeutic consequences such as treatment failure, similar minimum inhibitory concentration increases in antiseptic consumer products do not always coincide with failure.^{12,30} Additionally, studies of bacterial resistance to the antimicrobial ingredients used in consumer products are limited in number and are hindered by technical difficulties associated with the methods used to determine resistance to these agents because of their mode of action and patterns of use.^{12,30} For example, while antibiotics are prescribed for internal use and continuously maintained at an effective concentration within the body, the antimicrobials used in consumer products are used topically and over varying time periods and dosages. Thus, data on the emergence of bacteria resistant to the antimicrobial ingredients used in consumer products must be interpreted with these limitations in mind.

There are no data indicating resistance to triclocarban, but because the anilides have very little clinical application, this could also reflect lack of research interest in this group of compounds. With respect to the other common antimicrobial agents used in consumer products, the bis-phenols, QACs, and biguanides, mounting data indicate that acquired bacterial resistance to these agents is

increasing.^{12,30,32-38} Of particular importance is that preliminary indications suggest that acquired resistance to these antimicrobial products is due not only to mutations within the bacterial genome, but also to plasmid transfer.¹² The presence of resistance factors on plasmids that are transferable raises the possibility that once an organism becomes resistant, it may pass this resistance on to other bacteria as well.

Thus, data show that *Escherichia coli* possessing the plasmid R124, which alters the OmpF outer membrane protein, are more resistant to cetrime (a QAC) than *E coli* without the R124 plasmid.³⁹ Additionally, it has been shown that *Staphylococcus* strains carrying resistance plasmids to gentamicin also possess increased resistance to QACs, chlorhexidine, and other antimicrobial agents.^{38,40,41} This is because the genes responsible for gentamicin resistance encode proton-dependent export proteins that facilitate the efflux of the antibiotic from the bacteria. This same mechanism thus also provides the bacteria with resistance against QACs and chlorhexidine.^{42,43} This finding suggests that acquisition of resistance to antimicrobial agents such as QACs and chlorhexidine is probably due to preexisting resistance elements that developed as part of acquisition of resistance to antibiotics such as gentamicin. It thus can be argued that resistance to antimicrobial agents found in consumer products is unlikely to be due to their use in these products.

However, these data can also suggest that prolonged low-level exposure to antimicrobials like QACs and chlorhexidine may provide an environment that would select for organisms with efflux mechanisms that could then be adapted for use in resisting therapeutic antibiotics. This hypothesis is still being elucidated.¹² A recent study demonstrates that nontransferable resistance to chlorhexidine can be developed in *Pseudomonas stutzeri* by exposure to gradually increasing doses.³³ These resistant strains are also more resistant to triclosan and some antibiotics, although this varies from strain to strain. This finding suggests that resistance developed against one

antimicrobial may impart cross-resistance to another antimicrobial or antibiotic. While the resistance against chlorhexidine in this case was believed to be caused by alterations in the cell membrane, these data support the need for further research into the above-mentioned hypothesis.

A recent study³² reports the appearance of methicillin-resistant *Staphylococcus aureus* with increased resistance to triclosan, but more studies are needed to confirm this finding.³¹ This situation is of some concern owing to the widespread use of triclosan in clinical settings to reduce skin colonization with *Staphylococci* and because triclosan is used by many health care facilities in eradication procedures for methicillin-resistant *S aureus*.^{14,22-24} Resistance of other bacteria to triclosan has been reported,^{15,44} and the mechanism of such resistance has now been elucidated. As with resistance to QACs and chlorhexidine, 1 mechanism of resistance to triclosan is via overexpression of genes encoding positive regulators of a multidrug efflux pump or of the gene encoding the pump itself.³⁴ This facilitates efflux of the antimicrobial agent from the bacteria.

Triclosan exerts its effects by inhibiting the bacterial fatty acid synthesis at the enoyl-acyl carrier protein reductase step. Thus, the second mechanism of resistance to triclosan in *E coli* has been linked to a missense mutation in the gene that codes for the enoyl-acyl reductase protein.⁴⁵ This has also been documented in *Mycobacterium smegmatis*, in which resistance to triclosan is linked to mutations in the gene for an enoyl reductase required for fatty acid synthesis.⁴⁴ Significantly, this same study showed that 2 of 3 resistant strains also demonstrated some resistance to isoniazid, a common antibiotic used in the treatment of tuberculosis.⁴⁴

The absence of data supporting the efficacy of antimicrobial ingredients such as triclosan in household and consumer products suggests that they may be ineffective and therefore unnecessary. Published reports on acquired resistance to these antimicrobial agents, coupled with their increased use in consumer products, suggest that a

change may be occurring in the microbial flora of the home, specifically through the selection of resistant organisms.⁴⁶ Additionally, the possibility that the selection of organisms resistant to antimicrobials such as triclosan and chlorhexidine also may predispose these organisms to resistance against therapeutic antibiotics is troubling.^{31,47,48} Some data exist to support this concern, and research is continuing. It is unlikely, however, that resistance to therapeutic antibiotics resulting through this mechanism will prove to be a major factor in the current crisis in antibiotic resistance. Ultimately, health care practitioners must control antibiotic resistance through judicious use of these important drugs.

CONCLUSIONS

Despite the recent substantial increase in the use of antimicrobial ingredients in consumer products, the effects of this practice have not been studied extensively. No data support the efficacy or necessity of antimicrobial agents in such products, and a growing number of studies suggest increasing acquired bacterial resistance to them. Studies also suggest that acquired resistance to the antimicrobial agents used in consumer products may predispose bacteria to resistance against therapeutic antibiotics, but further research is needed. Many of these antimicrobial agents are used in the hospital setting to reduce surface colonization of bacteria, and this increased resistance may negatively affect such use. Studies also show that acquired bacterial resistance to antimicrobial agents used in consumer products may predispose the organisms to resistance against therapeutic antibiotics, but further research is needed. In light of these findings, there is little evidence to support the use of antimicrobial agents in consumer products such as topical hand lotions and soaps. However, there are insufficient studies to determine whether the use of antimicrobial agents in consumer products contributes to the general problem of increased resistance to therapeutic antibiotics. Considering the available data and the criti-

cal nature of the antibiotic resistance problem, it is prudent to avoid the use of antimicrobial agents in consumer products. Ultimately, antibiotic resistance is a major public health concern that also has to be controlled through changes in attitude toward, and more judicious use of, antibiotics by health care professionals and the public.

RECOMMENDATIONS

The following recommendations of the Council on Scientific Affairs were adopted by the American Medical Association in June 2000:

The American Medical Association

1. Encourages the Food and Drug Administration to expedite its regulation of the use in consumer products of antimicrobials for which acquired resistance has been demonstrated;
2. Will monitor the progress of the current Food and Drug Administration evaluation of the safety and effectiveness of antimicrobials for consumer use in over-the-counter hand and body washes; and
3. Encourages continued research on the use of common antimicrobials as ingredients in consumer products and its impact on the major public health problem of antimicrobial resistance.

Accepted for publication October 24, 2001.

This report was presented at the Interim Meeting of the American Medical Association, San Francisco, Calif, December 1-5, 2000. The recommendations were adopted as amended and the remainder of the report was filed.

Reprints: Barry Dickinson, PhD, Secretary to the Council on Scientific Affairs, American Medical Association, 515 N State St, Chicago, IL 60610 (e-mail: barry_dickinson@ama-assn.org).

REFERENCES

1. Shlaes DM, Gerding DN, John JF Jr, et al. Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals. *Clin Infect Dis*. 1997; 25:584-599.
2. Cohen FL, Tartasky D. Microbial resistance to drug therapy: a review. *Am J Infect Control*. 1997;25: 51-64.
3. Liu HH. Antibiotic resistance in bacteria: a current and future problem. *Adv Exp Med Biol*. 1999; 455:387-396.
4. Gould IM. A review of the role of antibiotic policies in the control of antibiotic resistance. *J Antimicrob Chemother*. 1999;43:459-465.
5. Rice LB. Successful interventions for gram-negative resistance to extended-spectrum beta-lactam antibiotics. *Pharmacotherapy*. 1999;19: 120S-128S.
6. Witte W. Antibiotic resistance in gram-positive bacteria: epidemiological aspects. *J Antimicrob Chemother*. 1999;44(suppl A):1-9.
7. Bradley SF. Issues in the management of resistant bacteria in long-term-care facilities. *Infect Control Hosp Epidemiol*. 1999;20:362-366.
8. Yates RR. New intervention strategies for reducing antibiotic resistance. *Chest*. 1999;115:24S-27S.
9. Okeke IN, Lamikanra A, Edelman R. Socioeconomic and behavioral factors leading to acquired bacterial resistance to antibiotics in developing countries. *Emerg Infect Dis*. 1999;5:18-27.
10. US Congress, Office of Technology Assessment. Impacts of antibiotic-resistant bacteria. Washington, DC: US Government Printing Office; 1995. Available at: <http://www.wws.princeton.edu/cgi-bin/byteserv.pr/ota/disk1/1995/9503/9503.PDF>. Accessed May 2, 2002.
11. World Health Organization. Containing antimicrobial resistance: review of the literature and report of a WHO workshop on the development of a global strategy for the containment of antimicrobial resistance. Geneva, Switzerland: World Health Organization; 1999. Available at: http://www.who.int/emc-documents/antimicrobial_resistance/whodscsrdrs992c.html. Accessed May 2, 2002.
12. McDonnell G, Russell AD. Antiseptics and disin-

Council on Scientific Affairs

Members and staff of the Council on Scientific Affairs, American Medical Association, at the time this report was prepared: *Members:* Myron Genel, MD (chair), New Haven, Conn; Michael A. Williams, MD, Baltimore, Md (chair-elect); Roy D. Altman, MD, Miami, Fla; Scott D. Deitchman, MD, MPH, Duluth, Ga; J. Chris Hawk III, MD, Charleston, SC; John P. Howe III, MD, San Antonio, Tex; Hillary D. Johnson, St Louis, Mo; Nancy H. Nielsen, MD, PhD, Buffalo, NY; John F. Schneider, MD, PhD, Chicago, Ill; Melvyn L. Sterling, MD, Orange, Calif; Zoltan Trizna, MD, PhD, Galveston, Tex; Donald C. Young, MD, Iowa City, Ia. *Staff:* Litjen Tan, PhD; Barry D. Dickinson, PhD (secretary); James M. Lyznicki, MS, MPH (assistant secretary); Marsha Meyer (editor), Chicago.

- fectants: activity, action, and resistance. *Clin Microbiol Rev.* 1999;12:147-179.
13. Faoagali JL, George N, Fong J, Davy J, Dowser M. Comparison of the antibacterial efficacy of 4% chlorhexidine gluconate and 1% triclosan hand-wash products in an acute clinical ward. *Am J Infect Control.* 1999;27:320-326.
 14. Irish D, Eltringham I, Teall A, et al. Control of an outbreak of an epidemic methicillin-resistant *Staphylococcus aureus* also resistant to mupirocin. *J Hosp Infect.* 1998;39:19-26.
 15. McMurry LM, Oethinger M, Levy SB. Triclosan targets lipid synthesis. *Nature.* 1998;394:531-532.
 16. Levy CW, Roujeinikova A, Sedelnikova S, et al. Molecular basis of triclosan activity. *Nature.* 1999;398:383-384.
 17. Ranganathan NS. Chlorhexidine. In: Ascenzi JM, ed. *Handbook of Disinfectants and Antiseptics.* New York, NY: Marcel Dekker Inc; 1996:235-264.
 18. Barrett-Bee K, Newbould L, Edwards S. The membrane destabilizing action of the antibacterial agent chlorhexidine. *FEMS Microbiol Lett.* 1994;119:249-254.
 19. 1997 APIC Guidelines Committee. The use of antimicrobial household products: APIC position statement. *APIC News.* 1997;16:13.
 20. Perencevich EN, Wong MT, Harris AD. National and regional assessment of the antibacterial soap market: a step toward determining the impact of prevalent antibacterial soaps. *Am J Infect Control.* 2001;29:281-283.
 21. Slater FM. Efficacy of triclosan: reply. *Am J Infect Control.* 1999;27:72-73.
 22. Harbarth S, Dharan S, Liassine N, Herrault P, Auckenthaler R, Pittet D. Randomized, placebo-controlled, double-blind trial to evaluate the efficacy of mupirocin for eradicating carriage of methicillin-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother.* 1999;43:1412-1416.
 23. Zafar AB, Butler RC, Reese DJ, Gaydos LA, Menonna PA. Use of 0.3% triclosan (Bacti-Stat) to eradicate an outbreak of methicillin-resistant *Staphylococcus aureus* in a neonatal nursery. *Am J Infect Control.* 1995;23:200-208.
 24. Webster J, Faoagali JL, Cartwright D. Elimination of methicillin-resistant *Staphylococcus aureus* from a neonatal intensive care unit after hand washing with triclosan. *J Paediatr Child Health.* 1994;30:59-64.
 25. Webster J. Handwashing in a neonatal intensive care nursery: product acceptability and effectiveness of chlorhexidine gluconate 4% and triclosan 1%. *J Hosp Infect.* 1992;21:137-141.
 26. Brady LM, Thomson M, Palmer MA, Harkness JL. Successful control of endemic MRSA in a cardiothoracic surgical unit. *Med J Aust.* 1990;152:240-245.
 27. Newsom SW, Rowland C. Studies on perioperative skin flora. *J Hosp Infect.* 1988;11(suppl B):21-26.
 28. Barry MA, Craven DE, Goularte TA, Lichtenberg DA. *Serratia marcescens* contamination of antiseptic soap containing triclosan: implications for nosocomial infection. *Infect Control.* 1984;5:427-430.
 29. Huang Y, Oie S, Kamiya A. Comparative effectiveness of hand-cleansing agents for removing methicillin-resistant *Staphylococcus aureus* from experimentally contaminated fingertips. *Am J Infect Control.* 1994;22:224-227.
 30. Jones RD. Bacterial resistance and topical antimicrobial wash products. *Am J Infect Control.* 1999;27:351-363.
 31. Russell AD. Bacterial resistance to disinfectants: present knowledge and future problems. *J Hosp Infect.* 1999;43(suppl):S57-S68.
 32. Bamber AI, Neal TJ. An assessment of triclosan susceptibility in methicillin-resistant and methicillin-sensitive *Staphylococcus aureus*. *J Hosp Infect.* 1999;41:107-109.
 33. Tattawasart U, Maillard JY, Furr JR, Russell AD. Development of resistance to chlorhexidine diacetate and cetylpyridinium chloride in *Pseudomonas stutzeri* and changes in antibiotic susceptibility. *J Hosp Infect.* 1999;42:219-229.
 34. McMurry LM, Oethinger M, Levy SB. Overexpression of *marA*, *soxS*, or *acrAB* produces resistance to triclosan in laboratory and clinical strains of *Escherichia coli*. *FEMS Microbiol Lett.* 1998;166:305-309.
 35. Sasatsu M, Shimizu K, Noguchi N, Kono M. Triclosan-resistant *Staphylococcus aureus*. *Lancet.* 1993;341:756.
 36. Cookson BD, Farrelly H, Stapleton P, Garvey RP, Price MR. Transferable resistance to triclosan in MRSA. *Lancet.* 1991;337:1548-1549.
 37. Cookson BD, Bolton MC, Platt JH. Chlorhexidine resistance in methicillin-resistant *Staphylococcus aureus* or just an elevated MIC? an in vitro and in vivo assessment. *Antimicrob Agents Chemother.* 1991;35:1997-2002.
 38. Sasatsu M, Shibata Y, Noguchi N, Kono M. High-level resistance to ethidium bromide and antiseptics in *Staphylococcus aureus*. *FEMS Microbiol Lett.* 1992;72:109-113.
 39. Rossouw FT, Rowbury RJ. Effects of the resistance plasmid R124 on the level of the OmpF outer membrane protein and on the response of *Escherichia coli* to environmental agents. *J Appl Bacteriol.* 1984;56:63-79.
 40. Russell AD. Plasmids and bacterial resistance to biocides. *J Appl Microbiol.* 1997;83:155-165.
 41. Littlejohn TG, Paulsen IT, Gillespie MT, et al. Substrate specificity and energetics of antiseptic and disinfectant resistance in *Staphylococcus aureus*. *FEMS Microbiol Lett.* 1992;74:259-265.
 42. Paulsen IT, Brown MH, Littlejohn TG, Mitchell BA, Skurray RA. Multidrug resistance proteins QacA and QacB from *Staphylococcus aureus*: membrane topology and identification of residues involved in substrate specificity. *Proc Natl Acad Sci U S A.* 1996;93:3630-3635.
 43. Paulsen IT, Littlejohn TG, Radstrom P, et al. The 3' conserved segment of integrons contains a gene associated with multidrug resistance to antiseptics and disinfectants. *Antimicrob Agents Chemother.* 1993;37:761-768.
 44. McMurry LM, McDermott PF, Levy SB. Genetic evidence that *InhA* of *Mycobacterium smegmatis* is a target for triclosan. *Antimicrob Agents Chemother.* 1999;43:711-713.
 45. Heath RJ, Rubin JR, Holland DR, Zhang E, Snow ME, Rock CO. Mechanism of triclosan inhibition of bacterial fatty acid synthesis. *J Biol Chem.* 1999;274:11110-11114.
 46. Levy SB, McMurry LM. Efficacy of triclosan [reply]. *Am J Infect Control.* 1999;27:73.
 47. Schweizer HP. Triclosan: a widely used biocide and its link to antibiotics. *FEMS Microbiol Lett.* 2001;202:1-7.
 48. Chuanchuen R, Beinlich K, Hoang TT, Becher A, Karkhoff-Schweizer RR, Schweizer HP. Cross-resistance between triclosan and antibiotics in *Pseudomonas aeruginosa* is mediated by multidrug efflux pumps: exposure of a susceptible mutant strain to triclosan selects *nfxB* mutants overexpressing MexCD-OprJ. *Antimicrob Agents Chemother.* 2001;45:428-432.

ARCHIVES Web Quiz Winner

Congratulations to the winner of our May quiz, Laura A. Finlayson, MD, FRCPC, Assistant Professor, Division of Dermatology, Dalhousie University, Bedford, Nova Scotia. The correct answer to our May challenge was *bullous mastocytosis*. For a complete discussion of this case, see the Off-Center Fold section in the June ARCHIVES (Chamlin SL, Cowper SE, Longley BJ, Williams ML. Generalized bullae in an infant. *Arch Dermatol.* 2002;138:831-836).

Be sure to visit the *Archives of Dermatology* World Wide Web site (<http://www.archdermatol.com>) to try your hand at the Interactive Quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month's print edition of the ARCHIVES. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also receive a free copy of the *The Art of JAMA II*.