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# Characterization of Mupirocin-Resistant *Staphylococcus aureus* from Different Geographic Areas

With the increasing use of mupirocin, resistance among staphylococci has emerged (1). High-level resistance (MICs, >500 μg/ml) is usually mediated by a plasmid-associated *mupA* gene. Low-level resistance (MICs, <100 μg/ml) is more common, can be selected in vitro with increasing concentrations of mupirocin, and, except for one report (7), has not been associated with *mupA*. We sought to define the characteristics and relatedness of Mup$^r$ strains from different geographic regions in the United States.

A total of 18 *Staphylococcus aureus* strains with high-level resistance (Hi-Mup$^r$ strains) and 19 *S. aureus* strains with low-level resistance (Lo-Mup$^r$ strains) were obtained from Ann Arbor, Mich.; Johnson City, Tenn.; and New Haven, Conn. (4–6, 8). Contour-clamped homogeneous electric field electrophoresis (CHEF) of genomic DNA was performed as described previously (7). Plasmid profile analysis was done following extraction of DNA by a rapid mini-prep procedure, treatment with *Hin*dIII, and separation of fragments by conventional agarose electrophoresis.

Southern analysis of chromosomal and plasmid DNA was performed according to standard procedures with a PCR-amplified product of an intragenic 1.65-kb *Nco*I fragment of *mupA* for the probe (7). Previously described oligonucleotide primers Mup1 and Mup2 were used for PCR amplifications (2). Filter mating experiments were carried out as described previously (3).

There were 11 Michigan strains (2 Hi-Mup$^r$ methicillin-resistant *S. aureus* [MRSA] and 9 Lo-Mup$^r$ [6 MRSA and 3 methicillin-susceptible *S. aureus*] strains), 14 Tennessee MRSA strains (6 Hi-Mup$^r$ and 8 Lo-Mup$^r$ strains), and 12 Connecticut strains (10 Hi-Mup$^r$ and 2 Lo-Mup$^r$ strains).

Eight different CHEF patterns were noted among the 37 strains. All 14 Tennessee strains were closely related and were similar to the 2 Hi-Mup$^r$ and to 5 of the 9 Lo-Mup$^r$ strains from Michigan; the 4 other Michigan strains showed three different patterns. Of the 12 Connecticut strains, 8 showed one predominant pattern and the other 4 showed three different patterns; all were unrelated to the Michigan and Tennessee strains.

All strains contained plasmids. Analysis of plasmid profiles showed differences between the Michigan and Tennessee strains that had appeared similar by CHEF typing; there were three different patterns among the 11 Michigan strains, and four entirely different patterns among the 14 Tennessee strains. The 12 strains from Connecticut showed five unique plasmid profiles.

All 18 Hi-Mup$^r$ strains transferred mupirocin resistance and contained *mupA* on plasmid DNA. The 2 Michigan strains carried *mupA* on a 9.1-kb fragment, the 6 Tennessee strains carried it on a 4.6- or a 5.5-kb fragment, and all 10 Connecticut strains carried it on a 4.6-kb fragment.

No Lo-Mup$^r$ strains transferred mupirocin resistance and, based on hybridization results, none had plasmid-associated *mupA*. In nine Michigan Lo-Mup$^r$ strains and two of eight Tennessee Lo-Mup$^r$ strains, the *mupA* probe hybridized to genomic DNA, indicating *mupA* is on the chromosome. No Connecticut Lo-Mup$^r$ strain showed hybridization to the *mupA* probe.

Both chromosomal and plasmid typing indicated that Connecticut strains were not related to Michigan and Tennessee strains. Although most of the strains from Michigan and Tennessee were closely related by CHEF typing, their plasmid profiles differed. Hi-Mup$^r$ *S. aureus* strains from the three geographic areas transferred resistance, but the plasmid location of the *mupA* gene varied.

Low-level mupirocin resistance was associated with chromosomal *mupA* in some but not all strains. Both high-level and low-level mupirocin resistance appeared to have arisen from multiple different clones within an individual institution and in different geographic areas of the United States.

## REFERENCES

1. **Bradley, S. F., M. A. Ramsey, T. M. Morton, and C. A. Kauffman.** 1995. Mupirocin resistance: clinical and molecular epidemiology. Infect. Control. Hosp. Epidemiol. **16:**354–358.
2. **Hodgson, J. E., S. P. Curnock, K. G. H. Dyke, R. Morris, D. R. Sylvester, and M. S. Gross.** 1994. Molecular characterization of the gene encoding high-level mupirocin resistance in *Staphylococcus aureus* J2870. Antimicrob. Agents Chemother. **38:**1205–1208.
3. **Janssen, D. A., L. T. Zarins, D. R. Schaberg, S. F. Bradley, M. S. Terpenning, and C. A. Kauffman.** 1993. Detection and characterization of mupirocin resistance in *Staphylococcus aureus*. Antimicrob. Agents Chemother. **37:**2003–2006.
4. **Kauffman, C. A., M. S. Terpenning, X. He, L. T. Zarins, M. A. Ramsey, K. A. Jorgenson, and S. F. Bradley.** 1993. Attempts to eradicate methicillin-resistant *Staphylococcus aureus* from a long-term care facility with the use of mupirocin ointment. Am. J. Med. **94:**371–378.
5. **Layton, M. C., and J. E. Patterson.** 1994. Mupirocin resistance among consecutive isolates of oxacillin-resistant and borderline oxacillin-resistant *Staphylococcus aureus* at a university hospital. Antimicrob. Agents Chemother. **38:**1664–1667.
6. **Layton, M. C., M. Perez, P. Heald, and J. E. Patterson.** 1993. An outbreak of mupirocin-resistant *Staphylococcus aureus* on a dermatology ward associated with an environmental reservoir. Infect. Control Hosp. Epidemiol. **14:**369–375.
7. **Ramsey, M. A., S. F. Bradley, C. A. Kauffman, and T. M. Morton.** 1996. Identification of chromosomal location of *mupA* gene encoding low-level mupirocin resistance in staphylococcal isolates. Antimicrob. Agents Chemother. **40:**2820–2823.
8. **Reagan, D. R., R. T. Dula, B. H. Palmer, C. N. Gutierrez, B. F. Franzus, and F. A. Sarubbi.** 1991. Control of MRSA in a VAMC with limited resources, abstr. 31, p. 104. *In* Program and abstracts of the 31st Interscience Conference on Antimicrobial Agents and Chemotherapy, American Society for Microbiology, Washington, D.C.

**Mary A. Ramsey**
**Suzanne F. Bradley**
**Carol A. Kauffman**
*Division of Infectious Diseases and Geriatric Medicine*
*Veterans Affairs Medical Center and University of Michigan Medical School*
*Ann Arbor, Michigan 48105*

**Teresa M. Morton**
*Department of Biology*
*Eastern Michigan University*
*Ypsilanti, Michigan*

**Jan E. Patterson**
*Division of Infectious Diseases*
*University of Texas at San Antonio and Audie Murphy Veterans Affairs Medical Center*
*San Antonio, Texas*

**David R. Reagan**
*Division of Infectious Diseases*
*East Tennessee State University Medical School and James H. Quillan Veterans Affairs Medical Center*
*Johnson City, Tennessee*