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TESIS DOCTORAL

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EPIDEMIOLOGÍA MOLECULAR Y RESISTENCIA A LOS ANTIMICROBIANOS EN *Staphylococcus* spp. EN CENTROS SANITARIOS DE MALLORCA DURANTE LOS ÚLTIMOS 15 AÑOS (1999-2013)

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CONCLUSIONES

7. CONCLUSIONES

1. Dos de los tres clones mayoritarios de SARM del HUSD durante el período 1999-2004 (los clones ST125-MRSA-IVc y ST228-MRSA-I) eran también los predominantes en muchos hospitales españoles, constatando la oligoclonalidad del SARM.

2. Por el contrario, el otro clon mayoritario de nuestro hospital (el ST22-MRSA-IVh, EMRSA-15) era prácticamente inexistente en el territorio peninsular español durante dicho período, aunque muy frecuente en otros países como el Reino Unido. Por tanto, el origen de este clon en Mallorca pudiera estar relacionado con el turismo británico en la isla.

3. Los tres clones mayoritarios del HUSD durante 2003-2004 fueron también los predominantes en los otros hospitales públicos de Mallorca, mostrando la importancia de la transmisión interhospitalaria.

4. A partir de 2007, de modo similar a la mayoría de hospitales españoles, se ha constatado en Mallorca la aparición del SARM comunitario. En 2008, el 7% de las cepas de SARM de los pacientes atendidos en el HUSD poseían los genes codificantes de la LPV. En todos los casos se trataron de infecciones de piel y partes blandas.

5. La práctica totalidad de las cepas de SARM productoras de LPV, al igual que sucede en el resto de España, pertenecían a los clones ST8-IVc (USA300-*like*) y ST8-IVa (USA300).

6. La prevalencia de portadores de SARM en exudados nasales de los residentes de un centro geriátrico de Mallorca fue del 8,0%, similar a la de otros estudios europeos, aunque menor que la descrita para otros centros asistenciales españoles.

7. La colonización por SARM en los residentes geriátricos fue generalmente transitoria, sin requerir intervenciones para su control.

8. Los factores de riesgo asociados con la colonización nasal de SARM en los residentes geriátricos fueron el tratamiento antibiótico en el último mes, el ingreso hospitalario previo, el presentar EPOC, y el antecedente de enfermedad vascular, enfermedad renal o neoplasia.

9. La mayoría de los residentes geriátricos colonizados por SARM no desarrollaron una infección subsiguiente por esta bacteria multirresistente. En los pocos casos en los que se constató una infección, se trataba de infecciones de herida o de úlcera, lo que indica que la colonización por SARM es un problema clínico manejable dentro de los centros socio-sanitarios.

10. Los clones de SARM en la residencia geriátrica fueron los mismos que los de su hospital de referencia. Ello pone de manifiesto la importancia de políticas de control de la infección coordinadas entre ambos tipos de instituciones.

11. En este trabajo se ha descrito por primera vez un plásmido de multirresistencia conjugativo (pERGB) portador de cuatro genes de resistencia: *cfr*, *ant(4')-Ia*, *tet*(L) y *dfrK*, detectado en SARM y *S. epidermidis*. Los múltiples regímenes de antibióticos administrados a estos pacientes podrían haber favorecido la formación y persistencia de este plásmido de multirresistencia.

12. Todas las cepas de *S. hominis* resistentes a la linezolida detectadas en dos hospitales de Mallorca pertenecían al mismo clon y presentaban la mutación G2576T en el gen ARNr 23S, lo cual sugiere la diseminación a través de pacientes transferidos entre los dos centros hospitalarios.

REFERENCIAS BIBLIOGRÁFICAS

8. REFERENCIAS BIBLIOGRÁFICAS

Abraham EP, Chain E. An enzyme from bacteria able to destroy penicillin. Nature. 1940; 146: 837.

Aires de Sousa M, Sanches IS, Ferro ML, Vaz MJ, Saraiva Z, Tendeiro T, Serra J, de Lencastre H. Intercontinental spread of a multidrug-resistant methicillin-resistant *Staphylococcus aureus* clone. J Clin Microbiol. 1998; 36: 2590-2596.

Aires-de-Sousa M, Conceição T, Simas C, de Lencastre H. Comparison of genetic backgrounds of methicillin-resistant and –susceptible *Staphylococcus aureus* isolates from Portuguese hospitals and the community. J Clin Microbiol. 2005; 43: 5150-5157.

Aires-de-Sousa M, Correia B, de Lencastre H; Multilaboratory Project Collaborators. Changing patterns in frequency of recovery of five methicillin-resistant *Staphylococcus aureus* clones in Portuguese hospitals: surveillance over a 16-year period. J Clin Microbiol. 2008; 46: 2912-2917.

Albrecht N, Jatzwauk L, Slickers P, Ehricht R, Monecke S. Clonal replacement of epidemic methicillin-resistant *Staphylococcus aureus* strains in a German university hospital over a period of eleven years. PLoS One. 2011; 6: e28189.

Albur MS, Bowker K, Weir I, MacGowan A. Factors influencing the clinical outcome of methicillin-resistant *Staphylococcus aureus* bacteraemia. Eur J Clin Microbiol Infect Dis. 2012; 31: 295-301.

Alcoceba E, Mena A, Pérez MC, Ruiz de Gopegui E, Padilla E, Gil J, Ramírez A, Gallegos MC, Serra A, Pérez JL, Oliver A. Molecular epidemiology of methicillin-resistant *Staphylococcus aureus* in Majorcan hospitals: high prevalence of the epidemic clone EMRSA-15. Clin Microbiol Infect. 2007; 13: 599-605.

Alm RA, McLaughlin RE, Kos VN, Sader HS, Iaconis JP, Lahiri SD. Analysis of *Staphylococcus aureus* clinical isolates with reduced susceptibility to ceftaroline: an epidemiological and structural perspective. J Antimicrob Chemother. 2014; 69: 2065-2075.

Álvarez CA, Barrientes OJ, Leal AL, Contreras GA, Barrero L, Rincón S, Díaz L, Vanegas N, Arias CA. Community-associated methicillin-resistant *Staphylococcus aureus*, Colombia. Emerg Infect Dis. 2006; 12: 2000-2001.

Álvarez-Lerma F, Palomar M, Olaechea P, Otal JJ, Insausti J, Cerdá E; Grupo de Estudio de Vigilancia de Infección Nosocomial en UCI. Estudio nacional de vigilancia de infección nosocomial en Unidades de Cuidados Intensivos. Informe evolutivo de los años 2003-2005. Med Intensiva. 2007; 31: 6-17.

Amorim ML, Faria NA, Oliveira DC, Vasconcelos C, Cabeda JC, Mendes AC, Calado E, Castro AP, Ramos MH, Amorim JM, de Lencastre H. Changes in the clonal nature and antibiotic resistance profiles of methicillin-resistant *Staphylococcus aureus* isolates associated with spread of the EMRSA-15 clone in a tertiary care Portuguese hospital. J Clin Microbiol. 2007; 45: 2881-2888.

Aparicio P, Richardson J, Martin S, Vindel A, Marples RR, Cookson BD. An epidemic methicillin-resistant strain of *Staphylococcus aureus* in Spain. Epidemiol Infect. 1992; 108: 287-298.

Archer NK, Mazaitis MJ, Costerton JW, Leid JG, Powers ME, Shirtliff ME. *Staphylococcus aureus* biofilms: properties, regulation, and roles in human disease. Virulence. 2011; 2: 445-459.

Arias CA, Rincón S, Chowdhury S, Martínez E, Coronell W, Reyes J, Nallapareddy SR, Murray BE. MRSA USA300 clone and VREF--a U.S.-Colombian connection? N Engl J Med. 2008a; 359: 2177-2179.

Arias CA, Vallejo M, Reyes J, Panesso D, Moreno J, Castañeda E, Villegas MV, Murray BE, Quinn JP. Clinical and microbiological aspects of linezolid resistance mediated by the *cfr* gene encoding a 23S rRNA methyltransferase. J Clin Microbiol. 2008b; 46: 892-896.

Ayliffe GA, Brightwell KM, Collins BJ, Lowbury EJ, Goonatilake PC, Etheridge RA. Surveys of hospital infection in the Birmingham region. I. Effect of age, sex, length of stay and antibiotic use on nasal carriage of tetracycline-resistant *Staphyloccus aureus* and on post-operative wound infection. J Hyg (Lond). 1977; 79: 299-314.

Babouee B, Frei R, Schultheiss E, Widmer AF, Goldenberger D. Comparison of the DiversiLab repetitive element PCR system with *spa* typing and pulsed-field gel electrophoresis for clonal characterization of methicillin-resistant *Staphylococcus aureus*. J Clin Microbiol. 2011; 49: 1549-1555.

Baldan R, Tassan Din C, Semeraro G, Costa C, Cichero P, Scarpellini P, Moro M, Cirillo DM. Severe community-onset infections in healthy individuals caused by community-acquired MRSA in an Italian teaching hospital, 2006-2008. J Hosp Infect. 2009; 72: 271-273.

Baos E, Candel FJ, Merino P, Pena I, Picazo JJ. Characterization and monitoring of linezolid-resistant clinical isolates of *Staphylococcus epidermidis* in an intensive care unit 4 years after an outbreak of infection by *cfr*-mediated linezolid-resistant *Staphylococcus aureus*. Diagn Microbiol Infect Dis. 2013; 76: 325-329.

Barber M, Rozwadowska-Dowzenko M. Infection by penicillin-resistant staphylococci. Lancet 1948; 2: 641-644.

Barber M. Methicillin-resistant staphylococci. J Clin Pathol 1961; 14: 385-393.

Barr B, Wilcox MH, Brady A, Parnell P, Darby B, Tompkins D. Prevalence of methicillin-resistant *Staphylococcus aureus* colonization among older residents of care homes in the United Kingdom. Infect Control Hosp Epidemiol. 2007; 28: 853-859.

Barrett FF, McGehee RF Jr, Finland M. Methicillin-resistant *Staphylococcus aureus* at Boston City Hospital. Bacteriologic and epidemiologic observations. N Engl J Med. 1968; 279: 441-448.

Barrett JF. Linezolid Pharmacia Corp. Curr Opin Investig Drugs. 2000; 1: 181-187.

Bastos MC, Murphy E. Transposon Tn*554* encodes three products required for transposition. EMBO J. 1988; 7: 2935-2941.

Becker K, Von Eiff C. *Staphylococcus, Micrococcus*, and other catalase-positive cocci. En Versalovic J, Carroll KC, Funke G, Jorgensen JH, Landry ML, Warnock DW (ed.). Manual of Clinical Microbiology. 10ª ed. Washington, DC: ASM Press, 2011; 308-330.

Begier EM, Frenette K, Barrett NL, Mshar P, Petit S, Boxrud DJ, Watkins-Colwell K, Wheeler S, Cebelinski EA, Glennen A, Nguyen D, Hadler JL; Connecticut Bioterrorism Field Epidemiology Response Team. A high-morbidity outbreak of methicillin-resistant *Staphylococcus aureus* among players on a college football team, facilitated by cosmetic body shaving and turf burns. Clin Infect Dis. 2004; 39: 1446-1453.

Berg T, Firth N, Apisiridej S, Hettiaratchi A, Leelaporn A, Skurray RA. Complete nucleotide sequence of pSK41: evolution of staphylococcal conjugative multiresistance plasmids. J Bacteriol. 1998; 180: 4350-4359.

Besier S, Ludwig A, Zander J, Brade V, Wichelhaus TA. Linezolid resistance in *Staphylococcus aureus*: gene dosage effect, stability, fitness costs, and cross-resistances. Antimicrob Agents Chemother. 2008; 52: 1570-1572.

Biedenbach DJ, Farrell DJ, Mendes RE, Ross JE, Jones RN. Stability of linezolid activity in an era of mobile oxazolidinone resistance determinants: results from the 2009 Zyvox® Annual Appraisal of Potency and Spectrum program. Diagn Microbiol Infect Dis. 2010; 68: 459-467.

Bisognano C, Kelley WL, Estoppey T, Francois P, Schrenzel J, Li D, Lew DP, Hooper DC, Cheung AL, Vaudaux P. A RecA-LexA-dependent pathway mediates ciprofloxacin-induced fibronectin binding in *Staphylococcus aureus*. J Biol Chem. 2004; 279: 9064-9071.

Blanco R, Tristán A, Ezpeleta G, Larsen AR, Bes M, Etienne J, Cisterna R, Laurent F. Molecular epidemiology of Panton-Valentine leukocidin-positive *Staphylococcus aureus* in Spain: emergence of the USA300 clone in an autochthonous population. J Clin Microbiol. 2011; 49: 433-436.

Bocchini CE, Hulten KG, Mason EO Jr, Gonzalez BE, Hammerman WA, Kaplan SL. Panton-Valentine leukocidin genes are associated with enhanced inflammatory response and local disease in acute hematogenous *Staphylococcus aureus* osteomyelitis in children. Pediatrics. 2006; 117: 433-440.

Bondi A Jr, Dietz C. Bacterial penicillinase; production, nature, and significance. J Bacteriol. 1946; 51: 125.

Bongiorno D, Campanile F, Mongelli G, Baldi MT, Provenzani R, Reali S, Lo Russo C, Santagati M, Stefani S. DNA methylase modifications and other linezolid resistance mutations in coagulase-negative staphylococci in Italy. J Antimicrob Chemother. 2010; 65: 2336-2340.

Bouza E, Martínez-Beltrán J, y Grupo de Trabajo para el Estudio de Estafilococos. Estudio multicéntrico sobre la prevalencia de estafilococos en España. Enferm Infecc Microbiol Clin 1988; 6: 68-79.

Bouza E, Muñoz P. Linezolid: pharmacokinetic characteristics and clinical studies. Clin Microbiol Infect. 2001; 7 (Suppl 4): 75-82.

Boyle-Vavra S, Daum RS. Community-acquired methicillin-resistant *Staphylococcus aureus*: the role of Panton-Valentine leukocidin. Lab Invest. 2007; 87: 3-9.

Bradley SF, Terpenning MS, Ramsey MA, Zarins LT, Jorgensen KA, Sottile WS, Schaberg DR, Kauffman CA. Methicillin-resistant *Staphylococcus aureus*: colonization and infection in a long-term care facility. Ann Intern Med. 1991; 115: 417-422.

Bradley SF. Methicillin-resistant *Staphylococcus aureus*: long-term care concerns. Am J Med. 1999; 106: 2S-10S.

Bradley SF. *Staphylococcus aureus* infections and antibiotic resistance in older adults. Clin Infect Dis. 2002; 34: 211-216.

Brakstad OG, Aasbakk K, Maeland JA. Detection of *Staphylococcus aureus* by polymerase chain reaction amplification of the *nuc* gene. J Clin Microbiol. 1992; 30: 1654-1660.

Broseta A, Chaves F, Rojo P, Otero JR. Emergencia de un clon de *Staphylococcus aureus* resistente a meticilina de origen comunitario en la población pediátrica del sur de Madrid. Enferm Infecc Microbiol Clin. 2006; 24: 31-35.

Bulger RJ. A methicillin-resistant strain of *Staphylococcus aureus*. Clinical and laboratory experience. Ann Intern Med. 1967; 67: 81-89.

Bullock WO, Fernández JM, Short, JM. XL-1 Blue: a high-efficiency plasmid transforming *recA Escherichia coli* strain with β-galactosidase selection. BioTechniques 1987; 5: 376-378.

Byrne ME, Gillespie MT, Skurray RA. 4',4'' adenyltransferase activity on conjugative plasmids isolated from *Staphylococcus aureus* is encoded on an integrated copy of pUB110. Plasmid. 1991; 25: 70-75.

Campanile F, Bongiorno D, Borbone S, Stefani S. Hospital-associated methicillin-resistant *Staphylococcus aureus* (HA-MRSA) in Italy. Ann Clin Microbiol Antimicrob. 2009; 8: 22.

Cañas-Pedrosa AM, Vindel A, Artiles F, Colino E, Lafarga B. Antimicrobial resistance and molecular epidemiology of Panton-Valentine leukocidin-positive community-associated methicillin-resistant *Staphylococcus aureus* from Gran Canaria (Canary Islands, Spain). Diagn Microbiol Infect Dis. 2012; 74: 432-434.

Carmona PM, Romá E, Monte E, García J, Gobernado M. Papel de linezolid en terapéutica antimicrobiana. Enferm Infecc Microbiol Clin. 2003; 21: 30-41.

Centers for Disease Control and Prevention (CDC). Four pediatric deaths from community-acquired methicillin-resistant *Staphylococcus aureus*--Minnesota and North Dakota, 1997-1999. MMWR Morb Mortal Wkly Rep. 1999; 48: 707-710.

Centers for Disease Control and Prevention (CDC). Methicillin-resistant *Staphylococcus aureus* skin or soft tissue infections in a state prison--Mississippi, 2000. MMWR Morb Mortal Wkly Rep. 2001; 50: 919-922.

Centers for Disease Control and Prevention (CDC). Methicillin-resistant *Staphylococcus aureus* infections among competitive sports participants--Colorado, Indiana, Pennsylvania, and Los Angeles County, 2000-2003. MMWR Morb Mortal Wkly Rep. 2003a; 52: 793-795.

Centers for Disease Control and Prevention (CDC). Methicillin-resistant *Staphylococcus aureus* infections in correctional facilities---Georgia, California, and Texas, 2001-2003. MMWR Morb Mortal Wkly Rep. 2003b; 52: 992-996.

Centers for Disease Control and Prevention (CDC). CDC reminds clinical laboratories and healthcare infection preventionists of their role in the search and containment of vancomycin-resistant *Staphylococcus aureus* (VRSA). 2010. http://www.cdc.gov/HAI/settings/lab/vrsa_lab_search_containment.html. Último acceso: 22/08/2012.

Cercenado E, Sánchez-Carrillo C, Alcalá L, Bouza E. Current status of resistance of *Staphylococcus* in Spain. 4th National Study (1996). Work Group on the Study of *Staphylococcus*. Rev Clin Esp. 1997; 197 (Suppl 2): 12-18.

Cercenado E, Cuevas O, Marín M, Bouza E, Trincado P, Boquete T, Padilla B, Vindel A. Community-acquired methicillin-resistant *Staphylococcus aureus* in Madrid, Spain: transcontinental importation and polyclonal emergence of Panton-Valentine leukocidin-positive isolates. Diagn Microbiol Infect Dis. 2008; 61: 143-149.

Cercenado E. Actualización en las resistencias de las bacterias grampositivas. Med Clin (Barc). 2010a; 135 (Suppl 3): 10-15.

Cercenado E, Marín M, Insa R, Bouza E. Emerging linezolid resistance: dissemination of the *cfr* gene among *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterococcus faecium* and *Enterococcus faecalis* and inability of the Etest method for detection. Abstract C2-1490. 50th Interscience Conference on Antimicrobial Agents and Chemotherapy. Boston, MA. USA. American Society for Microbiology. 2010b.

Chambers HF, Hartman BJ, Tomasz A. Increased amounts of a novel penicillin-binding protein in a strain of methicillin-resistant *Staphylococcus aureus* exposed to nafcillin. Clin Invest. 1985; 76: 325-331.

Chambers HF. The changing epidemiology of *Staphylococcus aureus*? Emerg Infect Dis. 2001; 7: 178-182.

Chang S, Sievert DM, Hageman JC, Boulton ML, Tenover FC, Downes FP, Shah S, Rudrik JT, Pupp GR, Brown WJ, Cardo D, Fridkin SK; Vancomycin-Resistant *Staphylococcus aureus* Investigative Team. Infection with vancomycin-resistant *Staphylococcus aureus* containing the *vanA* resistance gene. N Engl J Med. 2003; 348: 1342-1347.

Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40: 373-383.

Chaves F, García-Alvarez M, Sanz F, Alba C, Otero JR. Nosocomial spread of a *Staphylococcus hominis* subsp. *novobiosepticus* strain causing sepsis in a neonatal intensive care unit. J Clin Microbiol. 2005; 43: 4877-4879.

Chen FJ, Lauderdale TL, Huang IW, Lo HJ, Lai JF, Wang HY, Shiau YR, Chen PC, Ito T, Hiramatsu K. Methicillin-resistant *Staphylococcus aureus* in Taiwan. Emerg Infect Dis. 2005; 11: 1760-1763.

Chen HJ, Hung WC, Tseng SP, Tsai JC, Hsueh PR, Teng LJ. Fusidic acid resistance determinants in *Staphylococcus aureus* clinical isolates. Antimicrob Agents Chemother. 2010; 54: 4985-4991.

Chen H, Wu W, Ni M, Liu Y, Zhang J, Xia F, He W, Wang Q, Wang Z, Cao B, Wang H. Linezolid-resistant clinical isolates of enterococci and *Staphylococcus cohnii* from a multicentre study in China: molecular epidemiology and resistance mechanisms. Int J Antimicrob Agents. 2013; 42: 317-321.

Chung M, de Lencastre H, Matthews P, Tomasz A, Adamsson I, Aires de Sousa M, Camou T, Cocuzza C, Corso A, Couto I, Dominguez A, Gniadkowski M, Goering R, Gomes A, Kikuchi K, Marchese A, Mato R, Melter O, Oliveira D, Palacio R, Sá-Leão R, Santos Sanches I, Song JH, Tassios PT, Villari P; Multilaboratory Project Collaborators. Molecular typing of methicillin-resistant *Staphylococcus aureus* by pulsed-field gel electrophoresis: comparison of results obtained in a multilaboratory effort using identical protocols and MRSA strains. Microb Drug Resist. 2000; 6: 189-198.

Clinical Laboratory Standards Institute (CLSI). *Performance standards for antimicrobial susceptibility testing*; Nineteenth informational supplement. M100-S19. CLSI, Wayne, PA: CLSI document; 2009.

Clinical Laboratory Standards Institute (CLSI). *Performance standards for antimicrobial susceptibility testing*; Twenty-second informational supplement. M100-S22. CLSI, Wayne, PA: CLSI document; 2012.

Cobos-Trigueros N, Pitart C, Marco F, Martínez JA, Almela M, López J, Ortega M, Soriano A, Mensa J. Epidemiología y forma de presentación clínica de las infecciones originadas por *Staphylococcus aureus* resistente a meticilina productor de leucocidina de Panton-Valentine. Rev Esp Quimioter. 2010; 23: 93-99.

Collignon P, Gosbell I, Vickery A, Nimmo G, Stylianopoulos T, Gottlieb T. Community-acquired meticillin-resistant *Staphylococcus aureus* in Australia. Australian Group on Antimicrobial Resistance. Lancet. 1998; 352: 145-146.

Communicable Disease Report (CDR). Epidemic methicillin resistant *Staphylococcus aureus*. (Annon). Communicable Dis Rep. CDR Weekly 1996; 6: 197.

Cookson BD, Robinson DA, Monk AB, Murchan S, Deplano A, de Ryck R, Struelens MJ, Scheel C, Fussing V, Salmenlinna S, Vuopio-Varkila J, Cuny C, Witte W, Tassios PT, Legakis NJ, van Leeuwen W, van Belkum A, Vindel A, Garaizar J, Haeggman S, Olsson-Liljequist B, Ransjo U, Muller-Premru M, Hryniewicz W, Rossney A, O'Connell B, Short BD, Thomas J, O'Hanlon S, Enright MC. Evaluation of molecular typing methods in characterizing a European collection of epidemic methicillin-resistant *Staphylococcus aureus* strains: the HARMONY collection. J Clin Microbiol. 2007; 45: 1830-1837.

Coombs GW, Monecke S, Pearson JC, Tan HL, Chew YK, Wilson L, Ehricht R, O'Brien FG, Christiansen KJ. Evolution and diversity of community-associated methicillin-resistant *Staphylococcus aureus* in a geographical region. BMC Microbiol. 2011; 11: 215-227.

Corbella X, Domínguez MA, Pujol M, Ayats J, Sendra M, Pallarés R, Ariza J, Gudiol F. *Staphylococcus aureus* nasal carriage as a marker for subsequent staphylococcal infections in intensive care unit patients. Eur J Clin Microbiol Infect Dis. 1997; 16: 351-357.

Cox RA, Bowie PE. Methicillin-resistant *Staphylococcus aureus* colonization in nursing home residents: a prevalence study in Northamptonshire. J Hosp Infect. 1999; 43: 115-122.

Cribier B, Prévost G, Couppie P, Finck-Barbançon V, Grosshans E, Piémont Y. *Staphylococcus aureus* leukocidin: a new virulence factor in cutaneous infections? An epidemiological and experimental study. Dermatology. 1992; 185: 175-180.

Cuevas O, Cercenado E, Vindel A, Guinea J, Sánchez-Conde M, Sánchez-Somolinos M, Bouza E. Evolution of the antimicrobial resistance of *Staphylococcus* spp. in Spain: five nationwide prevalence studies, 1986 to 2002. Antimicrob Agents Chemother. 2004; 48: 4240-4245.

Cuevas O, Cercenado E, Bouza E, Castellares C, Trincado P, Cabrera R, Vindel A; Spanish Group for the Study of *Staphylococcus*. Molecular epidemiology of methicillin-resistant *Staphylococcus aureus* in Spain: a multicentre prevalence study (2002). Clin Microbiol Infect. 2007; 13: 250-256.

Cuevas O, Cercenado E, Goyanes MJ, Vindel A, Trincado P, Boquete T, Marín M, Bouza E; Grupo Español para el Estudio de Estafilococo. *Staphylococcus* spp. en España: situación actual y evolución de la resistencia a antimicrobianos (1986-2006). Enferm Infecc Microbiol Clin. 2008; 26: 269-277.

Cui L, Wang Y, Li Y, He T, Schwarz S, Ding Y, Shen J, Lv Y. Cfr-mediated linezolid-resistance among methicillin-resistant coagulase-negative Staphylococci from infections of humans. PLoS One. 2013; 8: e57096.

da Silva Coimbra MV, Silva-Carvalho MC, Wisplinghoff H, Hall GO, Tallent S, Wallace S, Edmond MB, Figueiredo AM, Wenzel RP. Clonal spread of methicillin-resistant *Staphylococcus aureus* in a large geographic area of the United States. J Hosp Infect. 2003; 53: 103-110.

Dai L, Wu CM, Wang MG, Wang Y, Wang Y, Huang SY, Xia LN, Li BB, Shen JZ. First report of the multidrug resistance gene *cfr* and the phenicol resistance gene *fexA* in a *Bacillus* strain from swine feces. Antimicrob Agents Chemother. 2010; 54: 3953-3955.

Dale GE, Broger C, D'Arcy A, Hartman PG, DeHoogt R, Jolidon S, Kompis I, Labhardt AM, Langen H, Locher H, Page MG, Stüber D, Then RL, Wipf B, Oefner C. A single amino acid substitution in *Staphylococcus aureus* dihydrofolate reductase determines trimethoprim resistance. J Mol Biol. 1997; 266: 23-30.

Das S, Anderson CJ, Grayes A, Mendoza K, Harazin M, Schora DM, Peterson LR. Nasal Carriage of Epidemic Methicillin-Resistant *Staphylococcus aureus* -15 (EMRSA-15) observed in three Chicago-area long term care facilities. Antimicrob Agents Chemother. 2013; 57: 4551–4553.

Daskalaki M, Otero JR, Chaves F. Molecular characterization of resistance to mupirocin in methicillin-resistant *Staphylococcus aureus* isolates in a tertiary hospital in Spain. J Antimicrob Chemother. 2009; 63: 826-828.

Daskalaki M, Rojo P, Marin-Ferrer M, Barrios M, Otero JR, Chaves F. Panton-Valentine leukocidin-positive *Staphylococcus aureus* skin and soft tissue infections among children in an emergency department in Madrid, Spain. Clin Microbiol Infect. 2010; 16: 74-77.

David MZ, Daum RS. Community-associated methicillin-resistant *Staphylococcus aureus*: epidemiology and clinical consequences of an emerging epidemic. Clin Microbiol Rev. 2010; 23: 616-687.

Davis KA, Stewart JJ, Crouch HK, Florez CE, Hospenthal DR. Methicillin-resistant *Staphylococcus aureus* (MRSA) nares colonization at hospital admission and its effect on subsequent MRSA infection. Clin Infect Dis. 2004; 39: 776-782.

de Almeida LM, de Araújo MR, Sacramento AG, Pavez M, de Souza AG, Rodrigues F, Gales AC, Lincopan N, Sampaio JL, Mamizuka EM. Linezolid resistance in Brazilian

Staphylococcus hominis strains is associated with L3 and 23S rRNA ribosomal mutations. Antimicrob Agents Chemother. 2013; 57: 4082-4083.

de Lencastre H, Tomasz A. Reassessment of the number of auxiliary genes essential for expression of high-level methicillin resistance in *Staphylococcus aureus*. Antimicrob Agents Chemother. 1994; 38: 2590-2598.

de Vries LE, Christensen H, Skov RL, Aarestrup FM, Agersø Y. Diversity of the tetracycline resistance gene *tet*(M) and identification of Tn*916*- and Tn*5801*- like (Tn*6014*) transposons in *Staphylococcus aureus* from humans and animals. J Antimicrob Chemother. 2009; 64: 490-500.

del Giudice P, Blanc V, de Rougemont A, Bes M, Lina G, Hubiche T, Roudière L, Vandenesch F, Etienne J. Primary skin abscesses are mainly caused by Panton-Valentine leukocidin-positive *Staphylococcus aureus* strains. Dermatology. 2009; 219: 299-302.

den Heijer CD, van Bijnen EM, Paget WJ, Pringle M, Goossens H, Bruggeman CA, Schellevis FG, Stobberingh EE; APRES Study Team. Prevalence and resistance of commensal *Staphylococcus aureus*, including meticillin-resistant *S. aureus*, in nine European countries: a cross-sectional study. Lancet Infect Dis. 2013; 13: 409-415.

Deurenberg RH, Stobberingh EE. The evolution of *Staphylococcus aureus*. Infect Genet Evol. 2008; 8: 747-763.

Diekema DJ, Richter SS, Heilmann KP, Dohrn CL, Riahi F, Tendolkar S, McDanel JS, Doern GV. Continued emergence of USA300 methicillin-resistant *Staphylococcus aureus* in the United States: results from a nationwide surveillance study. Infect Control Hosp Epidemiol. 2014; 35: 285-292.

Diep BA, Carleton HA, Chang RF, Sensabaugh GF, Perdreau-Remington F. Roles of 34 virulence genes in the evolution of hospital- and community-associated strains of methicillin-resistant *Staphylococcus aureus*. J Infect Dis. 2006a; 193: 1495-1503.

Diep BA, Gill SR, Chang RF, Phan TH, Chen JH, Davidson MG, Lin F, Lin J, Carleton HA, Mongodin EF, Sensabaugh GF, Perdreau-Remington F. Complete genome sequence of USA300, an epidemic clone of community-acquired meticillin-resistant *Staphylococcus aureus*. Lancet. 2006b; 367: 731-739.

Diep BA, Stone GG, Basuino L, Graber CJ, Miller A, des Etages SA, Jones A, Palazzolo-Ballance AM, Perdreau-Remington F, Sensabaugh GF, DeLeo FR, Chambers HF. The arginine catabolic mobile element and staphylococcal chromosomal cassette *mec* linkage: convergence of virulence and resistance in the USA300 clone of methicillin-resistant *Staphylococcus aureus*. J Infect Dis. 2008; 197: 1523-1530.

Diep BA, Chan L, Tattevin P, Kajikawa O, Martin TR, Basuino L, Mai TT, Marbach H, Braughton KR, Whitney AR, Gardner DJ, Fan X, Tseng CW, Liu GY, Badiou C, Etienne J, Lina G, Matthay MA, DeLeo FR, Chambers HF. Polymorphonuclear leukocytes mediate *Staphylococcus aureus* Panton-Valentine leukocidin-induced lung inflammation and injury. Proc Natl Acad Sci U S A. 2010; 107: 5587-5592.

Domínguez MA, de Lencastre H, Liñares J, Tomasz A. Spread and maintenance of a dominant methicillin-resistant *Staphylococcus aureus* (MRSA) clone during an outbreak of MRSA disease in a Spanish hospital. J Clin Microbiol. 1994; 32: 2081-2087.

ECDC. European Centre for Disease Prevention and Control (ECDC). European Antimicrobial Resistance Surveillance Nettwork (EARS-Net). Interactive database. Disponible en: http://www.ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx. Consultada el: 13/07/2014.

Ellington MJ, Yearwood L, Ganner M, East C, Kearns AM. Distribution of the ACME-*arcA* gene among methicillin-resistant *Staphylococcus aureus* from England and Wales. J Antimicrob Chemother. 2008; 61: 73-77.

Ellington MJ, Hope R, Livermore DM, Kearns AM, Henderson K, Cookson BD, Pearson A, Johnson AP. Decline of EMRSA-16 amongst methicillin-resistant *Staphylococcus aureus*

causing bacteraemias in the UK between 2001 and 2007. J Antimicrob Chemother. 2010; 65: 446-448.

Emori TG, Banerjee SN, Culver DH, Gaynes RP, Horan TC, Edwards JR, Jarvis WR, Tolson JS, Henderson TS, Martone WJ, *et al*. Nosocomial infections in elderly patients in the United States, 1986-1990. National Nosocomial Infections Surveillance System. Am J Med. 1991; 91: 289S-293S.

Ender M, McCallum N, Adhikari R, Berger-Bächi B. Fitness cost of SCC*mec* and methicillin resistance levels in *Staphylococcus aureus*. Antimicrob Agents Chemother. 2004; 48: 2295-2297.

Endimiani A, Blackford M, Dasenbrook EC, Reed MD, Bajaksouszian S, Hujer AM, Rudin SD, Hujer KM, Perreten V, Rice LB, Jacobs MR, Konstan MW, Bonomo RA. Emergence of linezolid-resistant *Staphylococcus aureus* after prolonged treatment of cystic fibrosis patients in Cleveland, Ohio. Antimicrob Agents Chemother. 2011; 55: 1684-1692.

Enright MC, Day NP, Davies CE, Peacock SJ, Spratt BG. Multilocus sequence typing for characterization of methicillin-resistant and methicillin-susceptible clones of *Staphylococcus aureus*. J Clin Microbiol. 2000; 38: 1008-1015.

Enright MC, Robinson DA, Randle G, Feil EJ, Grundmann H, Spratt BG. The evolutionary history of methicillin-resistant *Staphylococcus aureus* (MRSA). Proc Natl Acad Sci U S A. 2002; 99: 7687-7692.

Enright MC. The population structure of *Staphylococcus aureus*. En: Lindsay JA (ed.). *Staphylococcus*, Molecular genetics. Norfolk: Caister Academic Press, 2008; 29-43.

ENVIN-HELICS. Estudio nacional de vigilancia de infección nosocomial en servicios de Medicina Intensiva. Sociedad Española de Medicina Intensiva Crítica y Unidades Coronarias (SEMICYUC). Grupo de trabajo de Enfermedades Infecciosas. Disponible en: http://hws.vhebron.net/envin-helics/.

EPINE. Estudio de Prevalencia de las Infecciones Nosocomiales en España. Informe 2011. 22º Estudio. Sociedad Española de Medicina Preventiva, Salud Pública e Higiene.

EPINE-EPPS. Estudio de Prevalencia de las Infecciones Nosocomiales en España. Informe 2013. Sociedad Española de Medicina Preventiva, Salud Pública e Higiene.

Espadinha D, Faria NA, Miragaia M, Lito LM, Melo-Cristino J, de Lencastre H; Médicos Sentinela Network. Extensive dissemination of methicillin-resistant *Staphylococcus aureus* (MRSA) between the hospital and the community in a country with a high prevalence of nosocomial MRSA. PLoS One. 2013; 8: e59960.

Espejo E, Pons J, Riera A, Boada N, Simó M, Rueda J, Mérida D, Soler A, García Restoy E, Morera MA, Bella F. Prevalencia y características de la colonización por *Staphylococcus aureus* resistente a meticilina (SARM) en residencias de larga estancia. XII Congreso de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC). Valencia, 10-13 de mayo de 2006. Comunicación 621.

European Committee on Antimicrobial Susceptibility Testing (EUCAST). Breakpoint tables for interpretation of MICs and zone diameters. Versión 1.1. Abril 2010.

European Committee on Antimicrobial Susceptibility Testing (EUCAST). Breakpoint tables for interpretation of MICs and zone diameters. Versión 2.0. Enero 2012.

Euzéby JP. List of prokaryotic names with standing in nomenclature. Disponible en: http://www.bacterio.net/s/staphylococcus.html (consultada el 18/04/2012).

Eveillard M, Leroy C, Teissiere F, Lancien E, Branger C, de Lassence A, Joly-Guillou ML, Brun P. Impact of selective screening in the emergency department on meticillin-resistant *Staphylococcus aureus* control programmes. J Hosp Infect. 2006a; 63: 380-384.

Eveillard M, Mortier E, Lancien E, Lescure FX, Schmit JL, Barnaud G, Lenfant N, Vinceneux P, Joly-Guillou ML. Consideration of age at admission for selective screening to identify methicillin-resistant *Staphylococcus aureus* carriers to control dissemination in a medical ward. Am J Infect Control. 2006b; 34: 108-113.

Eveillard M, Charru P, Rufat P, Hippeaux MC, Lancien E, Benselama F, Branger C. Methicillin-resistant *Staphylococcus aureus* carriage in a long-term care facility: hypothesis about selection and transmission. Age Ageing. 2008; 37: 294-299.

Faria NA, Oliveira DC, Westh H, Monnet DL, Larsen AR, Skov R, de Lencastre H. Epidemiology of emerging methicillin-resistant *Staphylococcus aureus* (MRSA) in Denmark: a nationwide study in a country with low prevalence of MRSA infection. J Clin Microbiol. 2005; 43: 1836-1842.

Faria NA, Miragaia M, de Lencastre H; Multi Laboratory Project Collaborators. Massive dissemination of methicillin resistant *Staphylococcus aureus* in bloodstream infections in a high MRSA prevalence country: establishment and diversification of EMRSA-15. Microb Drug Resist. 2013; 19: 483-490.

Feβler A, Scott C, Kadlec K, Ehricht R, Monecke S, Schwarz S. Characterization of methicillin-resistant *Staphylococcus aureus* ST398 from cases of bovine mastitis. J Antimicrob Chemother. 2010; 65: 619-625.

Fisch J, Lansing B, Wang L, Symons K, Cherian K, McNamara S, Mody L. New acquisition of antibiotic-resistant organisms in skilled nursing facilities. J Clin Microbiol. 2012; 50: 1698-1703.

Flamm RK, Farrell DJ, Mendes RE, Ross JE, Sader HS, Jones RN. ZAAPS Program results for 2010: an activity and spectrum analysis of linezolid using clinical isolates from 75 medical centres in 24 countries. J Chemother. 2012; 24: 328-337.

Flamm RK, Mendes RE, Ross JE, Sader HS, Jones RN. An international activity and spectrum analysis of linezolid: ZAAPS Program results for 2011. Diagn Microbiol Infect Dis. 2013a; 76: 206-213.

Flamm RK, Mendes RE, Ross JE, Sader HS, Jones RN. Linezolid surveillance results for the United States: LEADER surveillance program 2011. Antimicrob Agents Chemother. 2013b; 57: 1077-1081.

Forbes BA, Sahm DF, Weissfeld, AS. Bacterial genetics, metabolism, and structure. En: Bailey & Scott's. Diagnostic Microbiology. 12ª ed. Philadelphia: Mosby Elsevier, 2007; 10-12.

Fossum AE, Bukholm G. Increased incidence of methicillin-resistant *Staphylococcus aureus* ST80, novel ST125 and SCC*mec*IV in the south-eastern part of Norway during a 12-year period. Clin Microbiol Infect. 2006; 12: 627-633.

Fournier B. Global regulators of *Staphylococcus aureus* virulence genes. En: Lindsay JA (ed.). *Staphylococcus*, Molecular genetics. Norfolk: Caister Academic Press, 2008; 131-137.

Fraise AP, Mitchell K, O'Brien SJ, Oldfield K, Wise R. Methicillin-resistant *Staphylococcus aureus* (MRSA) in nursing homes in a major UK city: an anonymized point prevalence survey. Epidemiol Infect. 1997; 118: 1-5.

Frénay HM, Theelen JP, Schouls LM, Vandenbroucke-Grauls CM, Verhoef J, van Leeuwen WJ, Mooi FR. Discrimination of epidemic and nonepidemic methicillin-resistant *Staphylococcus aureus* strains on the basis of protein A gene polymorphism. J Clin Microbiol. 1994; 32: 846-847.

Friedman ND, Kaye KS, Stout JE, McGarry SA, Trivette SL, Briggs JP, Lamm W, Clark C, MacFarquhar J, Walton AL, Reller LB, Sexton DJ. Health care--associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. Ann Intern Med. 2002; 137: 791-797.

Garazi M, Edwards B, Caccavale D, Auerbach C, Wolf-Klein G. Nursing homes as reservoirs of MRSA: myth or reality? J Am Med Dir Assoc. 2009; 10: 414-418.

García-Álvarez L, Holden MT, Lindsay H, Webb CR, Brown DF, Curran MD, Walpole E, Brooks K, Pickard DJ, Teale C, Parkhill J, Bentley SD, Edwards GF, Girvan EK, Kearns AM, Pichon B, Hill RL, Larsen AR, Skov RL, Peacock SJ, Maskell DJ, Holmes MA. Meticillin-resistant *Staphylococcus aureus* with a novel *mecA* homologue in human and bovine populations in the UK and Denmark: a descriptive study. Lancet Infect Dis. 2011; 11: 595-603.

García-Castellanos R, Mallorquí-Fernández G, Marrero A, Potempa J, Coll M, Gomis-Rüth FX. On the transcriptional regulation of methicillin resistance: MecI repressor in complex with its operator. J Biol Chem. 2004; 279: 17888-17896.

García-García JA, Santos-Morano J, Castro C, Bayoll-Serradilla E, Martín-Ponce ML, Vergara-López S, Martín-Rodríguez LM, Mateos-Gómez A, de la Cueva J, Martín-Mazuelos E, Gómez-Mateos JM, Corzo-Delgado JE. Prevalencia y factores asociados a la colonización por *Staphylococcus aureus* resistente a meticilina en centros de larga estancia en el sur de España. Enferm Infecc Microbiol Clin. 2011; 29: 405-410.

García-Garrote F, Cercenado E, Marín M, Bal M, Trincado P, Corredoira J, Ballesteros C, Pita J, Alonso P, Vindel A. Methicillin-resistant *Staphylococcus aureus* carrying the *mecC* gene: emergence in Spain and report of a fatal case of bacteraemia. J Antimicrob Chemother. 2014; 69: 45-50.

Gasch O, Ayats J, Angeles Dominguez M, Tubau F, Liñares J, Peña C, Grau I, Pallarés R, Gudiol F, Ariza J, Pujol M. Epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infection: secular trends over 19 years at a university hospital. Medicine (Baltimore). 2011; 90: 319-327.

Gasch O, Camoez M, Dominguez MA, Padilla B, Pintado V, Almirante B, Molina J, Lopez-Medrano F, Ruiz de Gopegui E, Martinez JA, Bereciartua E, Rodriguez-Lopez F, Fernandez-Mazarrasa C, Goenaga MA, Benito N, Rodriguez-Baño J, Espejo E, Pujol M; REIPI/GEIH Study Groups. Predictive factors for mortality in patients with methicillin-resistant

Staphylococcus aureus bloodstream infection: impact on outcome of host, microorganism and therapy. Clin Microbiol Infect. 2013; 19: 1049-1057.

Gasink LB, Lautenbach E. Prevention and treatment of health care-acquired infections. Med Clin North Am. 2008; 92: 295-313, viii.

Genestier AL, Michallet MC, Prévost G, Bellot G, Chalabreysse L, Peyrol S, Thivolet F, Etienne J, Lina G, Vallette FM, Vandenesch F, Genestier L. *Staphylococcus aureus* Panton-Valentine leukocidin directly targets mitochondria and induces Bax-independent apoptosis of human neutrophils. J Clin Invest. 2005; 115: 3117-3127.

Giannella M, Pinilla B, Capdevila JA, Martínez Alarcón J, Muñoz P, López Álvarez J, Bouza E; Estudio de Neumonía En Medicina Interna study Group from the Sociedad Española de Medicina Interna. Pneumonia treated in the internal medicine department: focus on healthcare-associated pneumonia. Clin Microbiol Infect. 2012; 18: 786-794.

Gillet Y, Issartel B, Vanhems P, Fournet JC, Lina G, Bes M, Vandenesch F, Piémont Y, Brousse N, Floret D, Etienne J. Association between *Staphylococcus aureus* strains carrying gene for Panton-Valentine leukocidin and highly lethal necrotising pneumonia in young immunocompetent patients. Lancet. 2002; 359: 753-759.

Girou E, Pujade G, Legrand P, Cizeau F, Brun-Buisson C. Selective screening of carriers for control of methicillin-resistant *Staphylococcus aureus* (MRSA) in high-risk hospital areas with a high level of endemic MRSA. Clin Infect Dis. 1998; 27: 543-550.

Goering RV, McDougal LK, Fosheim GE, Bonnstetter KK, Wolter DJ, Tenover FC. Epidemiologic distribution of the arginine catabolic mobile element among selected methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* isolates. J Clin Microbiol. 2007; 45: 1981-1984.

Gómez Rodríguez N, Ibáñez Ruán J, González M, Pintado A, Penelas Cortés Y. Artritis sépticas periféricas en adultos: Estudio epidemiológico en un área sanitaria gallega. An Med Interna. 2001; 18: 573-577.

Gómez MI, Lee A, Reddy B, Muir A, Soong G, Pitt A, Cheung A, Prince A. *Staphylococcus aureus* protein A induces airway epithelial inflammatory responses by activating TNFR1. Nat Med. 2004; 10: 842-848.

Gómez C, Daskalaki M, Otero JR, Chaves F. Factores de virulencia asociados a la cepa epidémica de *Staphylococcus aureus* resistente a meticilina (SARM) ST125-SCC*mec* tipo IV. XIII Reunión de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC). Sevilla, 3-5 de junio de 2009. Comunicación nº 221.

Gómez González C, Larrosa N, Ruiz de Gopegui E, Fernández A, Palacios A, Moraga F, Dueñas J, Suárez F, Barrios M, Chaves F, y Grupo de Infección por SARM en Pediatría. Infecciones por *Staphylococcus aureus* resistente a meticilina asociado a la comunidad en población pediátrica: estudio multicéntrico. XIV Congreso de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC). Barcelona, 19-22 de mayo de 2010. Comunicación 479.

Gómez-Sanz E, Torres C, Lozano C, Zarazaga M. High diversity of *Staphylococcus aureus* and *Staphylococcus pseudintermedius* lineages and toxigenic traits in healthy pet-owning household members. Underestimating normal household contact? Comp Immunol Microbiol Infect Dis. 2013; 36: 83-94.

González-Castillo J, Cenci C, Rodriguez-Adrada E, Candel FJ, de la Torre-Misiego F, Fernández C, Martín-Sánchez FJ. *Staphylococcus aureus* infections and factors associated with resistance to methicillin in a hospital emergency department. Rev Esp Quimioter. 2013; 26: 337-345.

Gorwitz RJ, Kruszon-Moran D, McAllister SK, McQuillan G, McDougal LK, Fosheim GE, Jensen BJ, Killgore G, Tenover FC, Kuehnert MJ. Changes in the prevalence of nasal

colonization with *Staphylococcus aureus* in the United States, 2001-2004. J Infect Dis. 2008; 197: 1226-1234.

Gosbell IB, Mercer JL, Neville SA, Chant KG, Munro R. Community-acquired, non-multiresistant oxacillin-resistant *Staphylococcus aureus* (NORSA) in South Western Sydney. Pathology. 2001; 33: 206-210.

Gosbell IB, Barbagiannakos T, Neville SA, Mercer JL, Vickery AM, O'Brien FG, Coombs GW, Malkowski MJ, Pearson JC. Non-multiresistant methicillin-resistant *Staphylococcus aureus* bacteraemia in Sydney, Australia: emergence of EMRSA-15, Oceania, Queensland and Western Australian MRSA strains. Pathology. 2006; 38: 239-244.

Gould IM, David MZ, Esposito S, Garau J, Lina G, Mazzei T, Peters G. New insights into meticillin-resistant *Staphylococcus aureus* (MRSA) pathogenesis, treatment and resistance. Int J Antimicrob Agents. 2012; 39: 96-104.

Grove TL, Benner JS, Radle MI, Ahlum JH, Landgraf BJ, Krebs C, Booker SJ. A radically different mechanism for S-adenosylmethionine-dependent methyltransferases. Science. 2011; 332: 604-607.

Grundmann H, Aanensen DM, van den Wijngaard CC, Spratt BG, Harmsen D, Friedrich AW; European Staphylococcal Reference Laboratory Working Group. Geographic distribution of *Staphylococcus aureus* causing invasive infections in Europe: a molecular-epidemiological analysis. PLoS Med. 2010; 7: e1000215.

Guignard B, Entenza JM, Moreillon P. Beta-lactams against methicillin-resistant *Staphylococcus aureus*. Curr Opin Pharmacol. 2005; 5: 479-489.

He T, Wang Y, Schwarz S, Zhao Q, Shen J, Wu C. Genetic environment of the multi-resistance gene *cfr* in methicillin-resistant coagulase-negative staphylococci from chickens, ducks, and pigs in China. Int J Med Microbiol. 2014; 304: 257-261.

Herold BC, Immergluck LC, Maranan MC, Lauderdale DS, Gaskin RE, Boyle-Vavra S, Leitch CD, Daum RS. Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. JAMA. 1998; 279: 593-598.

Hidalgo-García FI, Galarraga-Gay MC, Gómez-Fontanil M, Sáez-Nieto JA. *Staphylococcus aureus* subespecie *aureus* catalasa negativa: un nuevo caso en España. Enferm Infecc Microbiol Clin. 2011; 29: 708-709.

Hill RL, Kearns AM, Nash J, North SE, Pike R, Newson T, Woodford N, Calver R, Livermore DM. Linezolid-resistant ST36 methicillin-resistant *Staphylococcus aureus* associated with prolonged linezolid treatment in two paediatric cystic fibrosis patients. J Antimicrob Chemother. 2010; 65: 442-445.

Hiramatsu K, Aritaka N, Hanaki H, Kawasaki S, Hosoda Y, Hori S, Fukuchi Y, Kobayashi I. Dissemination in Japanese hospitals of strains of *Staphylococcus aureus* heterogeneously resistant to vancomycin. Lancet. 1997a; 350: 1670-1673.

Hiramatsu K, Hanaki H, Ino T, Yabuta K, Oguri T, Tenover FC. Methicillin-resistant *Staphylococcus aureus* clinical strain with reduced vancomycin susceptibility. J Antimicrob Chemother. 1997b; 40: 135-136.

Hirano N, Muroi T, Takahashi H, Haruki M. Site-specific recombinases as tools for heterologous gene integration. Appl Microbiol Biotechnol. 2011; 92: 227-239.

Holden MT, Feil EJ, Lindsay JA, Peacock SJ, Day NP, Enright MC, Foster TJ, Moore CE, Hurst L, Atkin R, Barron A, Bason N, Bentley SD, Chillingworth C, Chillingworth T, Churcher C, Clark L, Corton C, Cronin A, Doggett J, Dowd L, Feltwell T, Hance Z, Harris B, Hauser H, Holroyd S, Jagels K, James KD, Lennard N, Line A, Mayes R, Moule S, Mungall K, Ormond D, Quail MA, Rabbinowitsch E, Rutherford K, Sanders M, Sharp S, Simmonds M, Stevens K, Whitehead S, Barrell BG, Spratt BG, Parkhill J. Complete genomes of two clinical *Staphylococcus aureus* strains: evidence for the rapid evolution of virulence and drug resistance. Proc Natl Acad Sci U S A. 2004; 101: 9786-9791.

Holden MT, Lindsay JA. Whole genomes: sequence, microarray and systems biology. En: Lindsay JA (ed.). *Staphylococcus*, Molecular genetics. Norfolk: Caister Academic Press, 2008; 6-10.

Holden MT, Lindsay JA, Corton C, Quail MA, Cockfield JD, Pathak S, Batra R, Parkhill J, Bentley SD, Edgeworth JD. Genome sequence of a recently emerged, highly transmissible, multi-antibiotic- and antiseptic-resistant variant of methicillin-resistant *Staphylococcus aureus*, sequence type 239 (TW). J Bacteriol. 2010; 192: 888-892.

Holden MT, Hsu LY, Kurt K, Weinert LA, Mather AE, Harris SR, Strommenger B, Layer F, Witte W, de Lencastre H, Skov R, Westh H, Zemlicková H, Coombs G, Kearns AM, Hill RL, Edgeworth J, Gould I, Gant V, Cooke J, Edwards GF, McAdam PR, Templeton KE, McCann A, Zhou Z, Castillo-Ramírez S, Feil EJ, Hudson LO, Enright MC, Balloux F, Aanensen DM, Spratt BG, Fitzgerald JR, Parkhill J, Achtman M, Bentley SD, Nübel U. A genomic portrait of the emergence, evolution, and global spread of a methicillin-resistant *Staphylococcus aureus* pandemic. Genome Res. 2013; 23: 653-664.

Holmes NE, Turnidge JD, Munckhof WJ, Robinson JO, Korman TM, O'Sullivan MV, Anderson TL, Roberts SA, Gao W, Christiansen KJ, Coombs GW, Johnson PD, Howden BP. Antibiotic choice may not explain poorer outcomes in patients with *Staphylococcus aureus* bacteremia and high vancomycin minimum inhibitory concentrations. J Infect Dis. 2011; 204: 340-347.

Horner C, Parnell P, Hall D, Kearns A, Heritage J, Wilcox M. Meticillin-resistant *Staphylococcus aureus* in elderly residents of care homes: colonization rates and molecular epidemiology. J Hosp Infect. 2013; 83: 212-218.

Hsu CC, Macaluso CP, Special L, Hubble RH. High rate of methicillin resistance of *Staphylococcus aureus* isolated from hospitalized nursing home patients. Arch Intern Med. 1988; 148: 569-570.

Huang SS, Platt R. Risk of methicillin-resistant *Staphylococcus aureus* infection after previous infection or colonization. Clin Infect Dis. 2003; 36: 281-285.

Huijsdens XW, van Dijke BJ, Spalburg E, van Santen-Verheuvel MG, Heck ME, Pluister GN, Voss A, Wannet WJ, de Neeling AJ. Community-acquired MRSA and pig-farming. Ann Clin Microbiol Antimicrob. 2006; 5: 26.

International Working Group on the Classification of Staphylococcal Cassette Chromosome Elements (IWG-SCC). Classification of staphylococcal cassette chromosome *mec* (SCC*mec*): guidelines for reporting novel SCC*mec* elements. Antimicrob Agents Chemother. 2009; 53: 4961-4967.

Ito T, Katayama Y, Hiramatsu K. Cloning and nucleotide sequence determination of the entire *mec* DNA of pre-methicillin-resistant *Staphylococcus aureus* N315. Antimicrob Agents Chemother. 1999; 43: 1449-1458.

Ito T, Katayama Y, Asada K, Mori N, Tsutsumimoto K, Tiensasitorn C, Hiramatsu K. Structural comparison of three types of staphylococcal cassette chromosome *mec* integrated in the chromosome in methicillin-resistant *Staphylococcus aureus*. Antimicrob Agents Chemother. 2001; 45: 1323-1336.

Ito T, Hiramatsu K, Tomasz A, de Lencastre H, Perreten V, Holden MT, Coleman DC, Goering R, Giffard PM, Skov RL, Zhang K, Westh H, O'Brien F, Tenover FC, Oliveira DC, Boyle-Vavra S, Laurent F, Kearns AM, Kreiswirth B, Ko KS, Grundmann H, Sollid JE, John JF Jr, Daum R, Soderquist B, Buist G; International Working Group on the Classification of Staphylococcal Cassette Chromosome Elements (IWG-SCC). Guidelines for reporting novel *mecA* gene homologues. Antimicrob Agents Chemother. 2012; 56: 4997-4999.

Jessen O, Rosendal K, Bülow P, Faber V, Eriksen KR. Changing staphylococci and staphylococcal infections. A ten-year study of bacteria and cases of bacteremia. N Engl J Med. 1969; 281: 627-635.

Jevons MP. "Celbenin"-resistant staphylococci. BMJ 1961; i: 124-125.

Johnson AP, Aucken HM, Cavendish S, Ganner M, Wale MC, Warner M, Livermore DM, Cookson BD; UK EARSS participants. Dominance of EMRSA-15 and -16 among MRSA causing nosocomial bacteraemia in the UK: analysis of isolates from the European Antimicrobial Resistance Surveillance System (EARSS). J Antimicrob Chemother. 2001; 48: 143-144.

Johnson AP, Pearson A, Duckworth G. Surveillance and epidemiology of MRSA bacteraemia in the UK. J Antimicrob Chemother. 2005; 56: 455-462.

Johnson LB, Saeed S, Pawlak J, Manzor O, Saravolatz LD. Clinical and laboratory features of community-associated methicillin-resistant *Staphylococcus aureus*: is it really new? Infect Control Hosp Epidemiol. 2006; 27: 133-138.

Jones CH, Tuckman M, Howe AY, Orlowski M, Mullen S, Chan K, Bradford PA. Diagnostic PCR analysis of the occurrence of methicillin and tetracycline resistance genes among *Staphylococcus aureus* isolates from phase 3 clinical trials of tigecycline for complicated skin and skin structure infections. Antimicrob Agents Chemother. 2006; 50: 505-510.

Jones RN, Kohno S, Ono Y, Ross JE, Yanagihara K. ZAAPS International Surveillance Program (2007) for linezolid resistance: results from 5591 Gram-positive clinical isolates in 23 countries. Diagn Microbiol Infect Dis. 2009a; 64: 191-201.

Jones RN, Ross JE, Bell JM, Utsuki U, Fumiaki I, Kobayashi I, Turnidge JD. Zyvox Annual Appraisal of Potency and Spectrum program: linezolid surveillance program results for 2008. Diagn Microbiol Infect Dis. 2009b; 65: 404-413.

Jones RN, Flonta M, Gurler N, Cepparulo M, Mendes RE, Castanheira M. Resistance surveillance program report for selected European nations (2011). Diagn Microbiol Infect Dis. 2014; 78: 429-436.

Kadlec K, Schwarz S. Identification of a novel trimethoprim resistance gene, *dfrK*, in a methicillin-resistant *Staphylococcus aureus* ST398 strain and its physical linkage to the tetracycline resistance gene *tet*(L). Antimicrob Agents Chemother. 2009a; 53: 776-778.

Kadlec K, Schwarz S. Novel ABC transporter gene, *vga*(C), located on a multiresistance plasmid from a porcine methicillin-resistant *Staphylococcus aureus* ST398 strain. Antimicrob Agents Chemother. 2009b; 53: 3589-3591.

Kadlec K, Fessler AT, Hauschild T, Schwarz S. Novel and uncommon antimicrobial resistance genes in livestock-associated methicillin-resistant *Staphylococcus aureus*. Clin Microbiol Infect. 2012; 18: 745-755.

Kaminska KH, Purta E, Hansen LH, Bujnicki JM, Vester B, Long KS. Insights into the structure, function and evolution of the radical-SAM 23S rRNA methyltransferase Cfr that confers antibiotic resistance in bacteria. Nucleic Acids Res. 2010; 38: 1652-1663.

Kaneko J, Kimura T, Kawakami Y, Tomita T, Kamio Y. Panton-valentine leukocidin genes in a phage-like particle isolated from mitomycin C-treated *Staphylococcus aureus* V8 (ATCC 49775). Biosci Biotechnol Biochem 1997; 61: 1960-1962.

Katayama Y, Ito T, Hiramatsu K. A new class of genetic element, staphylococcus cassette chromosome *mec*, encodes methicillin resistance in *Staphylococcus aureus*. Antimicrob Agents Chemother. 2000; 44: 1549-1555.

Katayama Y, Ito T, Hiramatsu K. Genetic organization of the chromosome region surrounding *mecA* in clinical staphylococcal strains: role of IS*431*-mediated *mecI* deletion in expression of resistance in *mecA*-carrying, low-level methicillin-resistant *Staphylococcus haemolyticus*. Antimicrob Agents Chemother. 2001; 45: 1955-1963.

Katayama Y, Robinson DA, Enright MC, Chambers HF. Genetic background affects stability of *mecA* in *Staphylococcus aureus*. J Clin Microbiol. 2005; 43: 2380-2383.

Kazakova SV, Hageman JC, Matava M, Srinivasan A, Phelan L, Garfinkel B, Boo T, McAllister S, Anderson J, Jensen B, Dodson D, Lonsway D, McDougal LK, Arduino M, Fraser VJ, Killgore G, Tenover FC, Cody S, Jernigan DB. A clone of methicillin-resistant *Staphylococcus aureus* among professional football players. N Engl J Med. 2005; 352: 468-475.

Kehrenberg C, Ojo KK, Schwarz S. Nucleotide sequence and organization of the multiresistance plasmid pSCFS1 from *Staphylococcus sciuri*. J Antimicrob Chemother. 2004a; 54: 936-939.

Kehrenberg C, Schwarz S. *fexA*, a novel *Staphylococcus lentus* gene encoding resistance to florfenicol and chloramphenicol. Antimicrob Agents Chemother. 2004b; 48: 615-618.

Kehrenberg C, Schwarz S, Jacobsen L, Hansen LH, Vester B. A new mechanism for chloramphenicol, florfenicol and clindamycin resistance: methylation of 23S ribosomal RNA at A2503. Mol Microbiol. 2005; 57: 1064-1073.

Kehrenberg C, Schwarz S. Distribution of florfenicol resistance genes *fexA* and *cfr* among chloramphenicol-resistant *Staphylococcus* isolates. Antimicrob Agents Chemother. 2006; 50: 1156-1163.

Kehrenberg C, Aarestrup FM, Schwarz S. IS*21-558* insertion sequences are involved in the mobility of the multiresistance gene *cfr*. Antimicrob Agents Chemother. 2007; 51: 483-487.

Kehrenberg C, Cuny C, Strommenger B, Schwarz S, Witte W. Methicillin-resistant and -susceptible *Staphylococcus aureus* strains of clonal lineages ST398 and ST9 from swine carry the multidrug resistance gene *cfr*. Antimicrob Agents Chemother. 2009; 53: 779-781.

Kelly S, Collins J, Maguire M, Gowing C, Flanagan M, Donnelly M, Murphy PG. An outbreak of colonization with linezolid-resistant *Staphylococcus epidermidis* in an intensive therapy unit. J Antimicrob Chemother. 2008; 61: 901-907.

Kennedy AD, DeLeo FR. Epidemiology and virulence of community-associated MRSA. Clin Microb Newsl. 2009; 31: 153-160.

Kerr S, Kerr GE, Mackintosh CA, Marples RR. A survey of methicillin-resistant *Staphylococcus aureus* affecting patients in England and Wales. J Hosp Infect. 1990; 16: 35-48.

Kerttula AM, Lyytikäinen O, Vuopio-Varkila J, Ibrahem S, Agthe N, Broas M, Jägerroos H, Virolainen A. Molecular epidemiology of an outbreak caused by methicillin-resistant *Staphylococcus aureus* in a health care ward and associated nursing home. J Clin Microbiol. 2005; 43: 6161-6163.

Kirby WM. Extraction of a highly potent penicillin inactivator from penicillin resistant Staphylococci. Science. 1944; 99: 452-453.

Klappenbach JA, Saxman PR, Cole JR, Schmidt TM. rrndb: the Ribosomal RNA Operon Copy Number Database. Nucleic Acids Res. 2001; 29: 181-184.

Klevens RM, Morrison MA, Fridkin SK, Reingold A, Petit S, Gershman K, Ray S, Harrison LH, Lynfield R, Dumyati G, Townes JM, Craig AS, Fosheim G, McDougal LK, Tenover FC; Active Bacterial Core Surveillance of the Emerging Infections Program Network. Community-associated methicillin-resistant *Staphylococcus* aureus and healthcare risk factors. Emerg Infect Dis. 2006; 12: 1991-1993.

Klevens RM, Morrison MA, Nadle J, Petit S, Gershman K, Ray S, Harrison LH, Lynfield R, Dumyati G, Townes JM, Craig AS, Zell ER, Fosheim GE, McDougal LK, Carey RB, Fridkin SK; Active Bacterial Core surveillance (ABCs) MRSA Investigators. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. JAMA. 2007; 298: 1763-1771.

Kloos WE, Musselwhite MS. Distribution and persistence of *Staphylococcus* and *Micrococcus* species and other aerobic bacteria on human skin. Appl Microbiol. 1975; 30: 381-385.

Kluytmans J, Van Belkum A, Verbrugh H. Nasal carriage of *Staphylococcus aureus*: epidemiology, underlying mechanisms, and associated risks. Clin Microbiol Rev. 1997; 10: 505-520.

Knight GM, Budd EL, Lindsay JA. Large mobile genetic elements carrying resistance genes that do not confer a fitness burden in healthcare-associated meticillin-resistant *Staphylococcus aureus*. Microbiology. 2013; 159: 1661-1672.

Kobayashi N, Urasawa S, Uehara N, Watanabe N. Distribution of insertion sequence-like element IS*1272* and its position relative to methicillin resistance genes in clinically important Staphylococci. Antimicrob Agents Chemother. 1999; 43: 2780-2782.

Köseoğlu O, Sayın Kutlu S, Cevahir N. Prevalence and risk factors for methicillin-resistant *Staphylococcus aureus* colonization among outpatients undergoing hemodialysis treatment. Mikrobiyol Bul. 2012; 46: 106-112.

Kreiswirth B, Kornblum J, Arbeit RD, Eisner W, Maslow JN, McGeer A, Low DE, Novick RP. Evidence for a clonal origin of methicillin resistance in *Staphylococcus aureus*. Science. 1993; 259: 227-230.

Kuroda M, Ohta T, Uchiyama I, Baba T, Yuzawa H, Kobayashi I, Cui L, Oguchi A, Aoki K, Nagai Y, Lian J, Ito T, Kanamori M, Matsumaru H, Maruyama A, Murakami H, Hosoyama A, Mizutani-Ui Y, Takahashi NK, Sawano T, Inoue R, Kaito C, Sekimizu K, Hirakawa H, Kuhara S, Goto S, Yabuzaki J, Kanehisa M, Yamashita A, Oshima K, Furuya K, Yoshino C, Shiba T, Hattori M, Ogasawara N, Hayashi H, Hiramatsu K. Whole genome sequencing of meticillin-resistant *Staphylococcus aureus*. Lancet. 2001; 357: 1225-1240.

Lane DJ. 16S/23S rRNA sequencing. En: Stackebrandt E, Goodfellow M, editors. Nucleic acid techniques in bacterial systematics. Chichester: Wiley. 1991; 115-175.

Larsen A, Stegger M, Goering R, Sorum M, Skov R. Emergence and dissemination of the methicillin resistant *Staphylococcus aureus* USA300 clone in Denmark (2000-2005). Euro Surveill. 2007; 12: 22-24.

Lasseter G, Charlett A, Lewis D, Donald I, Howell-Jones R, McNulty CA. *Staphylococcus aureus* carriage in care homes: identification of risk factors, including the role of dementia. Epidemiol Infect. 2010; 138: 686-696.

Lauderdale TL, Wang JT, Lee WS, Huang JH, McDonald LC, Huang IW, Chang SC. Carriage rates of methicillin-resistant *Staphylococcus aureus* (MRSA) depend on anatomic location, the number of sites cultured, culture methods, and the distribution of clonotypes. Eur J Clin Microbiol Infect Dis. 2010; 29: 1553-1559.

Lazarevic V, Beaume M, Corvaglia A, Hernandez D, Schrenzel J, François P. Epidemiology and virulence insights from MRSA and MSSA genome analysis. Future Microbiol. 2011; 6: 513-532.

Le Goffic F, Martel A, Capmau ML, Baca B, Goebel P, Chardon H, Soussy CJ, Duval J, Bouanchaud DH. New plasmid-mediated nucleotidylation of aminoglycoside antibiotics in *Staphlococcus aureus*. Antimicrob Agents Chemother. 1976; 10: 258-264.

Leach KL, Brickner SJ, Noe MC, Miller PF. Linezolid, the first oxazolidinone antibacterial agent. Ann N Y Acad Sci. 2011; 1222: 49-54.

Lee SM, Ender M, Adhikari R, Smith JM, Berger-Bächi B, Cook GM. Fitness cost of staphylococcal cassette chromosome *mec* in methicillin-resistant *Staphylococcus aureus* by way of continuous culture. Antimicrob Agents Chemother. 2007; 51: 1497-1499.

Li S, Skov RL, Han X, Larsen AR, Larsen J, Sørum M, Wulf M, Voss A, Hiramatsu K, Ito T. Novel types of staphylococcal cassette chromosome *mec* elements identified in clonal complex 398 methicillin-resistant *Staphylococcus aureus* strains. Antimicrob Agents Chemother. 2011; 55: 3046-3650.

Lim TT, Chong FN, O'Brien FG, Grubb WB. Are all community methicillin-resistant *Staphylococcus aureus* related? A comparison of their *mec* regions. Pathology. 2003; 35: 336-343.

Lina G, Piémont Y, Godail-Gamot F, Bes M, Peter MO, Gauduchon V, Vandenesch F, Etienne J. Involvement of Panton-Valentine leukocidin-producing *Staphylococcus aureus* in primary skin infections and pneumonia. Clin Infect Dis. 1999; 29: 1128-1132.

Lindsay JA, Moore CE, Day NP, Peacock SJ, Witney AA, Stabler RA, Husain SE, Butcher PD, Hinds J. Microarrays reveal that each of the ten dominant lineages of *Staphylococcus aureus* has a unique combination of surface-associated and regulatory genes. J Bacteriol. 2006; 188: 669-676.

Lindsay JA. *S. aureus* evolution: lineages and mobile genetic elements (MGEs). En: Lindsay JA (ed.). *Staphylococcus*, Molecular genetics. Norfolk: Caister Academic Press, 2008; 46-69.

Lindsay JA. *Staphylococcus aureus* genomics and the impact of horizontal gene transfer. Int J Med Microbiol. 2014; 304: 103-109.

Lipinska U, Hermans K, Meulemans L, Dumitrescu O, Badiou C, Duchateau L, Haesebrouck F, Etienne J, Lina G. Panton-Valentine leukocidin does play a role in the early stage of *Staphylococcus aureus* skin infections: a rabbit model. PLoS One. 2011; 6: e22864.

Liu GY, Essex A, Buchanan JT, Datta V, Hoffman HM, Bastian JF, Fierer J, Nizet V. *Staphylococcus aureus* golden pigment impairs neutrophil killing and promotes virulence through its antioxidant activity. J Exp Med. 2005; 202: 209-215.

Liu L, Li Y, Zhang J, Zou W, Zhou Z, Liu J, Li X, Wang L, Chen J. Complete genome sequence of the industrial strain *Bacillus megaterium* WSH-002. J Bacteriol. 2011; 193: 6389-6390.

Livermore DM, James D, Reacher M, Graham C, Nichols T, Stephens P, Johnson AP, George RC. Trends in fluoroquinolone (ciprofloxacin) resistance in enterobacteriaceae from bacteremias, England and Wales, 1990-1999. Emerg Infect Dis. 2002; 8: 473-478.

Locke JB, Hilgers M, Shaw KJ. Mutations in ribosomal protein L3 are associated with oxazolidinone resistance in staphylococci of clinical origin. Antimicrob Agents Chemother. 2009; 53: 5275-5278.

Locke JB, Morales G, Hilgers M, G C K, Rahawi S, Picazo JJ, Shaw KJ, Stein JL. Elevated linezolid resistance in clinical *cfr*-positive *Staphylococcus aureus* isolates is associated with co-occurring mutations in ribosomal protein L3. Antimicrob Agents Chemother. 2010; 54: 5352-5355.

Locke JB, Rahawi S, LaMarre J, Mankin AS, Shaw KJ. Genetic environment and stability of *cfr* in methicillin-resistant *Staphylococcus aureus* CM05. Antimicrob Agents Chemother. 2012; 56: 332-340.

Locke JB, Zuill DE, Scharn CR, Deane J, Sahm DF, Denys GA, Goering RV, Shaw KJ. Linezolid-resistant *Staphylococcus aureus* strain 1128105, the first known clinical isolate possessing the *cfr* multidrug resistance gene. Antimicrob Agents Chemother. 2014; 58: 6592-6598.

Löffler B, Hussain M, Grundmeier M, Brück M, Holzinger D, Varga G, Roth J, Kahl BC, Proctor RA, Peters G. *Staphylococcus aureus* Panton-Valentine leukocidin is a very potent cytotoxic factor for human neutrophils. PLoS Pathog. 2010; 6: e1000715.

Long KS, Poehlsgaard J, Kehrenberg C, Schwarz S, Vester B. The Cfr rRNA methyltransferase confers resistance to phenicols, lincosamides, oxazolidinones, pleuromutilins, and streptogramin A antibiotics. Antimicrob Agents Chemother. 2006; 50: 2500-2505.

Lowy FD. Antimicrobial resistance: the example of *Staphylococcus aureus*. J Clin Invest. 2003; 111: 1265-1273.

Lozano C, Aspiroz C, Ara M, Gómez-Sanz E, Zarazaga M, Torres C. Methicillin-resistant *Staphylococcus aureus* (MRSA) ST398 in a farmer with skin lesions and in pigs of his farm: clonal relationship and detection of *lnu*(A) gene. Clin Microbiol Infect. 2011a; 17: 923-927.

Lozano C, Gómez-Sanz E, Benito D, Aspiroz C, Zarazaga M, Torres C. *Staphylococcus aureus* nasal carriage, virulence traits, antibiotic resistance mechanisms, and genetic lineages in healthy humans in Spain, with detection of CC398 and CC97 strains. Int J Med Microbiol. 2011b; 301: 500-505.

Lozano C, Rezusta A, Gómez P, Gómez-Sanz E, Báez N, Martín-Saco G, Zarazaga M, Torres C. High prevalence of *spa* types associated with the clonal lineage CC398 among tetracycline-resistant methicillin-resistant *Staphylococcus aureus* strains in a Spanish hospital. J Antimicrob Chemother. 2012a; 67: 330-334.

Lozano C, Ruiz-García M, Gómez-Sanz E, López-García P, Royo-García G, Zarazaga M, Torres C. Characterization of a *cfr*-positive methicillin-resistant *Staphylococcus epidermidis* strain of the lineage ST22 implicated in a life-threatening human infection. Diagn Microbiol Infect Dis. 2012b; 73: 380-382.

Lozano C, Aspiroz C, Gómez-Sanz E, Tirado G, Fortuño B, Zarazaga M, Torres C. Caracterización de cepas de *Staphylococcus epidermidis* y *S. haemolyticus* resistentes a meticilina y linezolid en un hospital español. Enferm Infecc Microbiol Clin. 2013a; 31: 136-141.

Lozano C, Porres-Osante N, Crettaz J, Rojo-Bezares B, Benito D, Olarte I, Zarazaga M, Sáenz Y, Torres C. Changes in genetic lineages, resistance, and virulence in clinical methicillin-resistant *Staphylococcus aureus* in a Spanish hospital. J Infect Chemother. 2013b; 19: 233-242.

Lyon BR, Skurray R. Antimicrobial resistance of *Staphylococcus aureus*: genetic basis. Microbiol Rev. 1987; 51: 88-134.

Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. Md State Med J. 1965; 14: 61-65.

Maiden MC, Bygraves JA, Feil E, Morelli G, Russell JE, Urwin R, Zhang Q, Zhou J, Zurth K, Caugant DA, Feavers IM, Achtman M, Spratt BG. Multilocus sequence typing: a portable approach to the identification of clones within populations of pathogenic microorganisms. Proc Natl Acad Sci U S A. 1998; 95: 3140-3145.

Malachowa N, Sabat A, Gniadkowski M, Krzyszton-Russjan J, Empel J, Miedzobrodzki J, Kosowska-Shick K, Appelbaum PC, Hryniewicz W. Comparison of multiple-locus variable-number tandem-repeat analysis with pulsed-field gel electrophoresis, *spa* typing, and multilocus sequence typing for clonal characterization of *Staphylococcus aureus* isolates. J Clin Microbiol. 2005; 43: 3095-3100.

Malachowa N, DeLeo FR. Mobile genetic elements of *Staphylococcus aureus*. Cell Mol Life Sci. 2010; 67: 3057-3071.

Mandell GL, Moorman DR. Treatment of experimental staphylococcal infections: effect of rifampin alone and in combination on development of rifampin resistance. Antimicrob Agents Chemother. 1980; 17: 658-662.

Manzur A, Vidal M, Pujol M, Cisnal M, Hornero A, Masuet C, Peña C, Gudiol F, Ariza J. Predictive factors of meticillin resistance among patients with *Staphylococcus aureus* bloodstream infections at hospital admission. J Hosp Infect. 2007; 66: 135-141.

Manzur A, Domínguez MA, Pujol M, González MP, Limon E, Hornero A, Martín R, Gudiol F, Ariza J. Community-acquired methicillin-resistant *Staphylococcus aureus* infections: an emerging threat in Spain. Clin Microbiol Infect. 2008a; 14: 377-380.

Manzur A, Gavaldà L, Ruiz de Gopegui E, Mariscal D, Domínguez MA, Pérez JL, Segura F, Pujol M; Group of the Spanish Network for Research in Infectious Diseases. Prevalence of

methicillin-resistant *Staphylococcus aureus* and factors associated with colonization among residents in community long-term-care facilities in Spain. Clin Microbiol Infect. 2008b; 14: 867-872.

Manzur A, Pujol M. Impacto y control de *Staphylococcus aureus* resistente a la meticilina (SARM) en los centros de larga estancia. Rev Esp Geriatr Gerontol. 2008c; 43: 235-238.

Manzur A, Domínguez MA, Ruiz de Gopegui E, Mariscal D, Gavaldà L, Segura F, Pérez JL, Pujol M; Spanish Network for Research in Infectious Diseases. Natural history of meticillin-resistant *Staphylococcus aureus* colonisation among residents in community long term care facilities in Spain. J Hosp Infect. 2010; 76: 215-219.

Manzur A, Ruiz de Gopegui E, Domínguez M, Mariscal D, Gavaldà L, Pérez JL, Segura F, Pujol M; Spanish Network for Research in Infectious Diseases. Clinical significance of methicillin-resistant *Staphylococcus aureus* colonization in residents in community long-term-care facilities in Spain. Epidemiol Infect. 2012; 140: 400-406.

March A, Aschbacher R, Dhanji H, Livermore DM, Böttcher A, Sleghel F, Maggi S, Noale M, Larcher C, Woodford N. Colonization of residents and staff of a long-term-care facility and adjacent acute-care hospital geriatric unit by multiresistant bacteria. Clin Microbiol Infect. 2010; 16: 934-44.

March A, Aschbacher R, Pagani E, Sleghel F, Soelva G, Hopkins KL, Doumith M, Innocenti P, Burth J, Piazzani F, Woodford N. Changes in colonization of residents and staff of a long-term care facility and an adjacent acute-care hospital geriatric unit by multidrug-resistant bacteria over a four-year period. Scand J Infect Dis. 2014; 46: 114-122.

Marimón JM, Villar M, García-Arenzana JM, Caba Ide L, Pérez-Trallero E. Molecular characterization of *Staphylococcus aureus* carrying the Panton-Valentine leucocidin genes in northern Spain. J Infect. 2012; 64: 47-53.

Marples RR, Reith S. Methicillin-resistant *Staphylococcus aureus* in England and Wales. Commun Dis Rep CDR Rev. 1992; 2: R25-29.

Masaki H, Watanabe H, Degawa S, Yoshimine H, Asoh N, Rikitomi N, Matsumoto K, Ahmed K, Watanabe K, Oishi K, Nagatake T. Significant reduction of methicillin-resistant *Staphylococcus aureus* bacteremia in geriatric wards after introduction of infection control measures against nosocomial infections. Intern Med. 2001; 40: 214-220.

Mazzariol A, Kocsis E, Bragagnolo L, Pellizzer G, Rassu M, Cornaglia G. Co-infection by two linezolid-resistant coagulase-negative staphylococci with two different resistance determinants. Scand J Infect Dis. 2012; 44: 978-981.

McDougal LK, Steward CD, Killgore GE, Chaitram JM, McAllister SK, Tenover FC. Pulsed-field gel electrophoresis typing of oxacillin-resistant *Staphylococcus aureus* isolates from the United States: establishing a national database. J Clin Microbiol. 2003; 41: 5113-5120.

McDougal LK, Fosheim GE, Nicholson A, Bulens SN, Limbago BM, Shearer JE, Summers AO, Patel JB. Emergence of resistance among USA300 methicillin-resistant *Staphylococcus aureus* isolates causing invasive disease in the United States. Antimicrob Agents Chemother. 2010; 54: 3804-3811.

McKenzie T, Hoshino T, Tanaka T, Sueoka N. Correction. A revision of the nucleotide sequence and functional map of pUB110. Plasmid. 1987; 17: 83-85.

McNeil SA, Mody L, Bradley SF. Methicillin-resistant *Staphylococcus aureus*. Management of asymptomatic colonization and outbreaks of infection in long-term care. Geriatrics. 2002; 57: 16-27.

Melter O, Aires de Sousa M, Laskafeldová K, Urbásková P, Wünschová M, de Lencastre H. Delineation of the endemic and sporadic methicillin-resistant *Staphylococcus aureus* clones in a Czech hospital. Microb Drug Resist. 2004; 10: 218-223.

Mendelson G, Yearmack Y, Granot E, Ben-Israel J, Colodner R, Raz R. *Staphylococcus aureus* carrier state among elderly residents of a long-term care facility. J Am Med Dir Assoc. 2003; 4: 125-127.

Mendes RE, Deshpande LM, Castanheira M, DiPersio J, Saubolle MA, Jones RN. First report of *cfr*-mediated resistance to linezolid in human staphylococcal clinical isolates recovered in the United States. Antimicrob Agents Chemother. 2008; 52: 2244-2246.

Mendes RE, Deshpande LM, Farrell DJ, Spanu T, Fadda G, Jones RN. Assessment of linezolid resistance mechanisms among *Staphylococcus epidermidis* causing bacteraemia in Rome, Italy. J Antimicrob Chemother. 2010; 65: 2329-2335.

Mendes RE, Deshpande LM, Bonilla HF, Schwarz S, Huband MD, Jones RN, Quinn JP. Dissemination of a pSCFS3-like *cfr*-carrying plasmid in *Staphylococcus aureus* and *Staphylococcus epidermidis* clinical isolates recovered from hospitals in Ohio. Antimicrob Agents Chemother. 2013; 57: 2923-2928.

Mendes RE, Hogan PA, Streit JM, Jones RN, Flamm RK. Zyvox(R) Annual Appraisal of Potency and Spectrum (ZAAPS) Program: report of linezolid activity over 9 years (2004-12). J Antimicrob Chemother. 2014; 69: 1582-1588.

Menegotto F, González-Cabrero S, Cubero Á, Cuervo W, Muñoz M, Gutiérrez MP, Simarro M, Bratos MÁ, Orduña A. Clonal nature and diversity of resistance, toxins and adhesins genes of meticillin-resistant *Staphylococcus aureus* collected in a Spanish hospital. Infect Genet Evol. 2012a; 12: 1751-1758.

Menegotto F, González-Cabrero S, Lorenzo B, Cubero Á, Cuervo W, Gutiérrez MP, Simarro M, Orduña A, Bratos MÁ. Molecular epidemiology of methicillin-resistant *Staphylococcus aureus* in a Spanish hospital over a 4-year period: clonal replacement decreased antimicrobial resistance, and identification of community-acquired and livestock-associated clones. Diagn Microbiol Infect Dis. 2012b; 74: 332-337.

Mermel LA, Cartony JM, Covington P, Maxey G, Morse D. Methicillin-resistant *Staphylococcus aureus* colonization at different body sites: a prospective, quantitative analysis. J Clin Microbiol. 2011; 49: 1119-1121.

Messing J, Gronenborn B, Müller-Hill B, Hans Hopschneider P. Filamentous coliphage M13 as a cloning vehicle: insertion of a *Hin*dII fragment of the *lac* regulatory region in M13 replicative form *in vitro*. Proc Natl Acad Sci U S A. 1977; 74: 3642-3646.

Mick V, Domínguez MA, Tubau F, Liñares J, Pujol M, Martín R. Molecular characterization of resistance to rifampicin in an emerging hospital-associated methicillin-resistant *Staphylococcus aureus* clone ST228, Spain. BMC Microbiol. 2010; 10: 68.

Milheiriço C, Oliveira DC, de Lencastre H. Multiplex PCR strategy for subtyping the staphylococcal cassette chromosome *mec* type IV in methicillin-resistant *Staphylococcus aureus*: 'SCC*mec* IV multiplex'. J Antimicrob Chemother. 2007a; 60: 42-48.

Milheiriço C, Oliveira DC, de Lencastre H. Update to the multiplex PCR strategy for assignment of *mec* element types in *Staphylococcus aureus*. Antimicrob Agents Chemother. 2007b; 51: 3374-3377.

Milisavljevic V, Wu F, Cimmotti J, Haas J, Della-Latta P, Larson E, Saiman L. Genetic relatedness of *Staphylococcus epidermidis* from infected infants and staff in the neonatal intensive care unit. Am J Infect Control. 2005; 33: 341-347.

Mitchell JM, MacCulloch D, Morris AJ. MRSA in the community. N Z Med J. 1996; 109: 411.

Mody L, Flannery E, Bielaczyc A, Bradley SF. Molecular epidemiology of *Staphylococcus aureus* colonization in 2 long-term care facilities. Infect Control Hosp Epidemiol. 2006; 27: 212-214.

Moet GJ, Jones RN, Biedenbach DJ, Stilwell MG, Fritsche TR. Contemporary causes of skin and soft tissue infections in North America, Latin America, and Europe: Report from the SENTRY Antimicrobial Surveillance Program (1998-2004). Diagn Microbiol Infect Dis 2007; 57: 7-13.

Monecke S, Jatzwauk L, Weber S, Slickers P, Ehricht R. DNA microarray-based genotyping of methicillin-resistant *Staphylococcus aureus* strains from Eastern Saxony. Clin Microbiol Infect. 2008; 14: 534-545.

Monecke S, Ehricht R, Slickers P, Tan HL, Coombs G. The molecular epidemiology and evolution of the Panton-Valentine leukocidin-positive, methicillin-resistant *Staphylococcus aureus* strain USA300 in Western Australia. Clin Microbiol Infect. 2009; 15: 770-776.

Monecke S, Stieber B, Roberts R, Akpaka PE, Slickers P, Ehricht R. Population structure of *Staphylococcus aureus* from Trinidad & Tobago. PLoS One. 2014; 9: e89120.

Montgomery CP, Boyle-Vavra S, Daum RS. The arginine catabolic mobile element is not associated with enhanced virulence in experimental invasive disease caused by the community-associated methicillin-resistant *Staphylococcus aureus* USA300 genetic background. Infect Immun. 2009; 77: 2650-2656.

Moore PC, Lindsay JA. Molecular characterisation of the dominant UK methicillin-resistant *Staphylococcus aureus* strains, EMRSA-15 and EMRSA-16. J Med Microbiol. 2002; 51: 516-521.

Morales G, Picazo JJ, Baos E, Candel FJ, Arribi A, Peláez B, Andrade R, de la Torre MA, Fereres J, Sánchez-García M. Resistance to linezolid is mediated by the *cfr* gene in the first report of an outbreak of linezolid-resistant *Staphylococcus aureus*. Clin Infect Dis. 2010; 50: 821-825.

Moran GJ, Krishnadasan A, Gorwitz RJ, Fosheim GE, McDougal LK, Carey RB, Talan DA; EMERGEncy ID Net Study Group. Methicillin-resistant *S. aureus* infections among patients in the emergency department. N Engl J Med. 2006; 355: 666-674.

Morgan M, Evans-Williams D, Salmon R, Hosein I, Looker DN, Howard A. The population impact of MRSA in a country: the national survey of MRSA in Wales, 1997. J Hosp Infect. 2000; 44: 227-239.

Morosini MI, Cantón R. Tolerancia y heterorresistencia en microorganismos grampositivos. Med Clin (Barc). 2010; 135 (Suppl 3): 16-22.

Morrison MA, Hageman JC, Klevens RM. Case definition for community-associated methicillin-resistant *Staphylococcus aureus*. J Hosp Infect. 2006; 62: 241.

Muder RR, Brennen C, Wagener MM, Vickers RM, Rihs JD, Hancock GA, Yee YC, Miller JM, Yu VL. Methicillin-resistant staphylococcal colonization and infection in a long-term care facility. Ann Intern Med. 1991; 114: 107-112.

Mulanovich VE, Huband MD, McCurdy SP, Lemmon MM, Lescoe M, Jiang Y, Rolston KV, LaSala PR. Emergence of linezolid-resistant coagulase-negative *Staphylococcus* in a cancer centre linked to increased linezolid utilization. J Antimicrob Chemother. 2010; 65: 2001-2004.

Mulhausen PL, Harrell LJ, Weinberger M, Kochersberger GG, Feussner JR. Contrasting methicillin-resistant *Staphylococcus aureus* colonization in Veterans Affairs and community nursing homes. Am J Med. 1996; 100: 24-31.

Murchan S, Kaufmann ME, Deplano A, de Ryck R, Struelens M, Zinn CE, Fussing V, Salmenlinna S, Vuopio-Varkila J, El Solh N, Cuny C, Witte W, Tassios PT, Legakis N, van Leeuwen W, van Belkum A, Vindel A, Laconcha I, Garaizar J, Haeggman S, Olsson-Liljequist B, Ransjo U, Coombes G, Cookson B. Harmonization of pulsed-field gel electrophoresis protocols for epidemiological typing of strains of methicillin-resistant *Staphylococcus aureus*: a single approach developed by consensus in 10 European laboratories and its application for tracing the spread of related strains. J Clin Microbiol. 2003; 41: 1574-1585.

Murphy E, Lin SL, Nunez L, Andrew L, Fink PS, Dilts DA, Hoiseth SK, Jansen KU, Anderson AS. Challenges for the evaluation of *Staphylococcus aureus* protein based vaccines: monitoring antigenic diversity. Hum Vaccin. 2011; 7 (Suppl): 51-59.

Murphy CR, Eells SJ, Quan V, Kim D, Peterson E, Miller LG, Huang SS. Methicillin-resistant *Staphylococcus aureus* burden in nursing homes associated with environmental contamination of common areas. J Am Geriatr Soc. 2012a; 60: 1012-1018.

Murphy CR, Quan V, Kim D, Peterson E, Whealon M, Tan G, Evans K, Meyers H, Cheung M, Lee BY, Mukamel DB, Huang SS. Nursing home characteristics associated with methicillin-resistant *Staphylococcus aureus* (MRSA) burden and transmission. BMC Infect Dis. 2012b; 12: 269.

Murray PR, Rosenthal KS, Pfaller MA. *Staphylococcus* y cocos grampositivos relacionados. En: Murray PR, Rosenthal KS, Pfaller MA (ed.). Microbiología médica. 7ª edición. Barcelona: Elsevier Saunders, 2013; 177.

Musser JM, Kapur V. Clonal analysis of methicillin-resistant *Staphylococcus aureus* strains from intercontinental sources: association of the *mec* gene with divergent phylogenetic lineages implies dissemination by horizontal transfer and recombination. J Clin Microbiol. 1992; 30: 2058-2063.

Mutnick AH, Enne V, Jones RN. Linezolid resistance since 2001: SENTRY Antimicrobial Surveillance Program. Ann Pharmacother. 2003; 37: 769-774.

Ng EY, Trucksis M, Hooper DC. Quinolone resistance mutations in topoisomerase IV: relationship to the *flqA* locus and genetic evidence that topoisomerase IV is the primary target and DNA gyrase is the secondary target of fluoroquinolones in *Staphylococcus aureus*. Antimicrob Agents Chemother. 1996; 40: 1881-1888.

Nimmo GR, Coombs GW, Pearson JC, O'Brien FG, Christiansen KJ, Turnidge JD, Gosbell IB, Collignon P, McLaws ML. Methicillin-resistant *Staphylococcus aureus* in the Australian community: an evolving epidemic. Med J Aust. 2006; 184: 384-388.

Nimmo GR. USA300 abroad: global spread of a virulent strain of community-associated methicillin-resistant *Staphylococcus aureus*. Clin Microbiol Infect. 2012; 18: 725-734.

Nissen M, Marshall H, Richmond P, Shakib S, Jiang Q, Cooper D, Rill D, Baber J, Eiden J, Gruber W, Jansen KU, Emini EA, Anderson AS, Zito ET, Girgenti D. A randomized phase I study of the safety and immunogenicity of three ascending dose levels of a 3-antigen *Staphylococcus aureus* vaccine (SA3Ag) in healthy adults. Vaccine. 2015; 33: 1846-1854.

Nouwen JL, Ott A, Kluytmans-Vandenbergh MF, Boelens HA, Hofman A, van Belkum A, Verbrugh HA. Predicting the *Staphylococcus aureus* nasal carrier state: derivation and validation of a "culture rule". Clin Infect Dis. 2004; 39: 806-811.

Nouwen J, Schouten J, Schneebergen P, Snijders S, Maaskant J, Koolen M, van Belkum A, Verbrugh HA. *Staphylococcus aureus* carriage patterns and the risk of infections associated with continuous peritoneal dialysis. J Clin Microbiol. 2006; 44: 2233-2236.

Novick RP. Analysis by transduction of mutations affecting penicillinase formation in *Staphylococcus aureus*. J Gen Microbiol. 1963; 33: 121-136.

Nübel U, Dordel J, Kurt K, Strommenger B, Westh H, Shukla SK, Zemlicková H, Leblois R, Wirth T, Jombart T, Balloux F, Witte W. A timescale for evolution, population expansion, and spatial spread of an emerging clone of methicillin-resistant *Staphylococcus aureus*. PLoS Pathog. 2010; 6: e1000855.

O'Brien L, Kerrigan SW, Kaw G, Hogan M, Penadés J, Litt D, Fitzgerald DJ, Foster TJ, Cox D. Multiple mechanisms for the activation of human platelet aggregation by *Staphylococcus aureus*: roles for the clumping factors ClfA and ClfB, the serine-aspartate repeat protein SdrE and protein A. Mol Microbiol. 2002; 44: 1033-1044.

Ogston A. *Micrococcus* poisoning. J Anat Physiol 1883; 17: 24-58.

Oliveira DC, de Lencastre H. Multiplex PCR strategy for rapid identification of structural types and variants of the *mec* element in methicillin-resistant *Staphylococcus aureus*. Antimicrob Agents Chemother. 2002a; 46: 2155-2161.

Oliveira DC, Tomasz A, de Lencastre H. Secrets of success of a human pathogen: molecular evolution of pandemic clones of meticillin-resistant *Staphylococcus aureus*. Lancet Infect Dis. 2002b; 2: 180-189.

Olsen RH, DeBusscher G, McCombie WR. Development of broad-host-range vectors and gene banks: self-cloning of the *Pseudomonas aeruginosa* PAO chromosome. J Bacteriol. 1982; 150: 60-69.

O'Sullivan NP, Keane CT. Risk factors for colonization with methicillin-resistant *Staphylococcus aureus* among nursing home residents. J Hosp Infect. 2000a; 45: 206-210.

O'Sullivan NP, Keane CT. The prevalence of methicillin-resistant *Staphylococcus aureus* among the residents of six nursing homes for the elderly. J Hosp Infect. 2000b; 45: 322-329.

Oteo J, Cruchaga S, Campos J, Sáez JA, Baquero F, y miembros españoles del Grupo del *European Antimicrobial Resistance System* (EARSS). Resistencia a antibióticos en *Staphylococcus aureus* aislados de sangre en 31 hospitales españoles de la Red Europea de Vigilancia de Resistencia a Antibióticos (2000). Med Clin (Barc). 2002; 119: 361-365.

Otter JA, French GL. The emergence of community-associated methicillin-resistant *Staphylococcus aureus* at a London teaching hospital, 2000-2006. Clin Microbiol Infect. 2008; 14: 670-676.

Pang Y, Bosch T, Roberts MC. Single polymerase chain reaction for the detection of tetracycline-resistant determinants Tet K and Tet L. Mol Cell Probes. 1994; 8: 417-422.

Panton P, Valentine F. Staphylococcal toxins. Lancet. 1932; 222: 506-508.

Park C, Shin HH, Kwon EY, Choi SM, Kim SH, Park SH, Choi JH, Yoo JH, Lee DG, Shin WS. Two variants of staphylococcal cassette chromosome *mec* type IVA in community-associated meticillin-resistant *Staphylococcus aureus* strains in South Korea. J Med Microbiol. 2009; 58: 1314-1321.

Parker MT, Jevons MP. A survey of methicillin resistance in *Staphylococcus aureus*. Postgrad Med J. 1964; 40 (Suppl): 170-178.

Parras F, Rodríguez M, Bouza E, Muñoz P, Cercenado E, Guerrero C, Zancada G. Brote epidémico de *Staphylococcus aureus* resistente a meticilina (SARM) en un hospital general. Informe preliminar. Enferm Infecc Microbiol Clin. 1991; 9: 200-207.

Pastagia M, Kleinman LC, Lacerda de la Cruz EG, Jenkins SG. Predicting risk for death from MRSA bacteremia. Emerg Infect Dis. 2012; 18: 1072-1080.

Pearman JW, Coombs GW, Grubb WB, O'Brien F. A British epidemic strain of methicillin-resistant *Staphylococcus aureus* (UK EMRSA-15) in Western Australia. Med J Aust. 2001; 174: 662.

Pérez-Jorge C, Isea-Peña MC, Heili S, Esteban J. Spread of *cfr* gene among staphylococci conferring resistance to linezolid in a patient under treatment. J Antibiot (Tokyo). 2012; 65: 151-152.

Pérez-Roth E, Lorenzo-Díaz F, Batista N, Moreno A, Méndez-Alvarez S. Tracking methicillin-resistant *Staphylococcus aureus* clones during a 5-year period (1998 to 2002) in a Spanish hospital. J Clin Microbiol. 2004; 42: 4649-4656.

Pérez-Roth E, Potel-Alvarellos C, Espartero X, Constela-Caramés L, Méndez-Álvarez S, Alvarez-Fernández M. Molecular epidemiology of plasmid-mediated high-level mupirocin resistance in methicillin-resistant *Staphylococcus aureus* in four Spanish health care settings. Int J Med Microbiol. 2013; 303: 201-204.

Pérez-Trallero E, García Arenzana J, Castañeda AA, Grisolia LP. Unusual multiresistant *Staphylococcus aureus* in a newborn nursery. Am J Dis Child. 1981; 135: 689-692.

Pérez-Trallero E, García Arenzana JM, Cilla Eguiluz G, Cisterna Cáncer R. Prevalence of methicillin-resistant *Staphylococcus aureus* in a Spanish hospital. Rev Infect Dis. 1988; 10: 627-628.

Pérez-Vázquez M, Vindel A, Marcos C, Oteo J, Cuevas O, Trincado P, Bautista V, Grundmann H, Campos J; EARSS Spain *spa*-typing Group. Spread of invasive Spanish *Staphylococcus aureus spa*-type t067 associated with a high prevalence of the aminoglycoside-modifying enzyme gene *ant(4')-Ia* and the efflux pump genes *msrA*/*msrB*. J Antimicrob Chemother. 2009; 63: 21-31.

Pfingsten-Würzburg S, Pieper DH, Bautsch W, Probst-Kepper M. Prevalence and molecular epidemiology of meticillin-resistant *Staphylococcus aureus* in nursing home residents in northern Germany. J Hosp Infect. 2011; 78: 108-112.

Picazo JJ, Betriu C, Rodríguez-Avial I, Culebras E, Gómez M; Grupo VIRA. Vigilancia de resistencias a los antimicrobianos: estudio VIRA 2004. Enferm Infecc Microbiol Clin. 2004; 22: 517-525.

Picazo JJ, Betriu C, Rodríguez-Avial I, Culebras E, Gómez M, López F; Grupo VIRA. Vigilancia de resistencias a los antimicrobianos: estudio VIRA 2006. Enferm Infecc Microbiol Clin. 2006; 24: 617-628.

Picazo JJ, Betriu C, Rodríguez-Avial I, Culebras E, López F, Gómez M; Grupo VIRA. Actividad comparativa de la daptomicina frente a *Staphylococcus aureus* resistente a meticilina y frente a estafilococos coagulasa negativa. Enferm Infecc Microbiol Clin. 2010; 28: 13-16.

Picazo JJ, Betriu C, Rodríguez-Avial I, Culebras E, López-Fabal F, Gómez M; VIRA Study Group. Comparative activities of daptomycin and several agents against staphylococcal blood isolates. Glycopeptide tolerance. Diagn Microbiol Infect Dis. 2011; 70: 373-379.

Pinho MG. Mechanisms of β-lactam and glycopeptide resistance in *Staphylococcus aureus.* En: Lindsay JA (ed.). *Staphylococcus*, Molecular genetics. Norfolk: Caister Academic Press, 2008; 216-226.

Plata K, Rosato AE, Wegrzyn G. *Staphylococcus aureus* as an infectious agent: overview of biochemistry and molecular genetics of its pathogenicity. Acta Biochim Pol. 2009; 56: 597-612.

Porrero MC, Valverde A, Fernández-Llario P, Díez-Guerrier A, Mateos A, Lavín S, Cantón R, Fernández-Garayzabal JF, Domínguez L. *Staphylococcus aureus* carrying *mecC* gene in animals and urban wastewater, Spain. Emerg Infect Dis. 2014; 20: 899-901.

Potoski BA, Adams J, Clarke L, Shutt K, Linden PK, Baxter C, Pasculle AW, Capitano B, Peleg AY, Szabo D, Paterson DL. Epidemiological profile of linezolid-resistant coagulase-negative staphylococci. Clin Infect Dis. 2006; 43:165-171.

Prévost G, Pottecher B, Dahlet M, Bientz M, Mantz JM, Piémont Y. Pulsed field gel electrophoresis as a new epidemiological tool for monitoring methicillin-resistant *Staphylococcus aureus* in an intensive care unit. J Hosp Infect. 1991; 17: 255-269.

Prieto-Pérez L, Pérez-Tanoira R, Petkova-Saiz E, Pérez-Jorge C, López-Rodríguez C, Álvarez-Álvarez B, Polo-Sabau J, Esteban J. Osteomyelitis: a descriptive study. Clin Orthop Surg. 2014; 6: 20-25.

Proctor RA. Role of folate antagonists in the treatment of methicillin-resistant *Staphylococcus aureus* infection. Clin Infect Dis. 2008; 46: 584-593.

Pujol M. Importancia de los centros geriátricos o de las instituciones sanitarias de estancia prolongada en la persistencia de la endemia por SARM. Enferm Infecc Microbiol Clin. 2011; 29: 403-404.

Que YA, Moreillon P. *Staphylococcus aureus* (incluido el síndrome del shock tóxico). En: Mandell GL, Bennett JE, Dolin R (ed.). Enfermedades Infecciosas, Principios y Práctica. 7ª ed. Barcelona: Elsevier, 2012; 2543-2582.

Queck SY, Otto M. *Staphylococcus epidermidis* and other Coagulase-Negative Staphylococci. En: Lindsay JA (ed.). *Staphylococcus*, Molecular genetics. Norfolk: Caister Academic Press, 2008; 227-254.

Quiles-Melero I, Gómez-Gil R, Romero-Gómez MP, Sánchez-Díaz AM, de Pablos M, García-Rodriguez J, Gutiérrez A, Mingorance J. Mechanisms of linezolid resistance among Staphylococci in a tertiary hospital. J Clin Microbiol. 2013; 51: 998-1001.

Rammelkamp CH, Maxon T. Resistance of *Staphylococcus aureus* of the action of penicillin. Proc. Royal Soc. Exper. Biol. Med. 1942; 51: 386–389.

Renzoni A, Andrey DO, Jousselin A, Barras C, Monod A, Vaudaux P, Lew D, Kelley WL. Whole genome sequencing and complete genetic analysis reveals novel pathways to glycopeptide resistance in *Staphylococcus aureus*. PLoS One. 2011; 6: e21577.

Reyes J, Rincón S, Díaz L, Panesso D, Contreras GA, Zurita J, Carrillo C, Rizzi A, Guzmán M, Adachi J, Chowdhury S, Murray BE, Arias CA. Dissemination of methicillin-resistant *Staphylococcus aureus* USA300 sequence type 8 lineage in Latin America. Clin Infect Dis. 2009; 49: 1861-1867.

Reynolds R, Hope R, Warner M, Macgowan AP, Livermore DM, Ellington MJ; on behalf of the BSAC Extended Working Party on Resistance Surveillance. Lack of upward creep of glycopeptide MICs for methicillin-resistant *Staphylococcus aureus* (MRSA) isolated in the UK and Ireland 2001-07. J Antimicrob Chemother. 2012; 67: 2912-2918.

Rice LB, Bonomo RA. Mechanisms of resistance to antibacterial agents. En: Versalovic J, Carroll KC, Funke G, Jorgensen JH, Landry ML, Warnock DW (ed.). Manual of Clinical Microbiology. 10ª ed. Washington, DC: ASM Press, 2011; 1082-1114.

Richardson JF, Reith S. Characterization of a strain of methicillin-resistant *Staphylococcus aureus* (EMRSA-15) by conventional and molecular methods. J Hosp Infect. 1993; 25: 45-52.

Robinson DA, Enright MC. Evolutionary models of the emergence of methicillin-resistant *Staphylococcus aureus*. Antimicrob Agents Chemother. 2003; 47: 3926-3934.

Rodríguez-Aranda A, Daskalaki M, Villar J, Sanz F, Otero JR, Chaves F. Nosocomial spread of linezolid-resistant *Staphylococcus haemolyticus* infections in an intensive care unit. Diagn Microbiol Infect Dis. 2009; 63: 398-402.

Rodríguez-Baño J, Bischofberger C, Alvarez-Lerma F, Asensio A, Delgado T, García-Arcal D, García-Ortega L, Hernández MJ, Molina-Cabrillana J, Pérez-Canosa C, Pujol M; M. Pujol and Grupos de Estudio de Infección Hospitalaria (GEIH) and de Infección en el Paciente Crítico (GEIPC) of Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC) and Sociedad Española de Medicina Preventiva, Salud Pública e Higiene (SEMPSPH). Vigilancia y control de *Staphylococcus aureus* resistente a meticilina en hospitales españoles. Documento de consenso GEIH-SEIMC y SEMPSPH. Enferm Infecc Microbiol Clin. 2008; 26: 285-298.

Rodríguez-Baño J, Domínguez MA, Millán AB, Borraz C, González MP, Almirante B, Cercenado E, Padilla B, Pujol M; GEIH/GEMARA (SEIMC); REIPI. Clinical and molecular epidemiology of community-acquired, healthcare-associated and nosocomial methicillin-resistant *Staphylococus aureus* in Spain. Clin Microbiol Infect. 2009; 15: 1111-1118.

Rodríguez-Baño J, López-Prieto MD, Portillo MM, Retamar P, Natera C, Nuño E, Herrero M, del Arco A, Muñoz A, Téllez F, Torres-Tortosa M, Martín-Aspas A, Arroyo A, Ruiz A, Moya R, Corzo JE, León L, Pérez-López JA; SAEI/SAMPAC Bacteraemia Group. Epidemiology and clinical features of community-acquired, healthcare-associated and nosocomial bloodstream infections in tertiary-care and community hospitals. Clin Microbiol Infect. 2010; 16: 1408-1413.

Roghmann MC, Siddiqui A, Plaisance K, Standiford H. MRSA colonization and the risk of MRSA bacteraemia in hospitalized patients with chronic ulcers. J Hosp Infect. 2001; 47: 98-103.

Rojas L, Bunsow E, Muñoz P, Cercenado E, Rodríguez-Créixems M, Bouza E. Vancomycin MICs do not predict the outcome of methicillin-resistant *Staphylococcus aureus* bloodstream infections in correctly treated patients. J Antimicrob Chemother. 2012; 67: 1760-1768.

Rojo P, Barrios M, Palacios A, Gomez C, Chaves F. Community-associated *Staphylococcus aureus* infections in children. Expert Rev Anti Infect Ther. 2010; 8: 541-554.

Rolain JM, François P, Hernandez D, Bittar F, Richet H, Fournous G, Mattenberger Y, Bosdure E, Stremler N, Dubus JC, Sarles J, Reynaud-Gaubert M, Boniface S, Schrenzel J, Raoult D. Genomic analysis of an emerging multiresistant *Staphylococcus aureus* strain rapidly spreading in cystic fibrosis patients revealed the presence of an antibiotic inducible bacteriophage. Biol Direct. 2009; 4: 1.

Rolo J, Miragaia M, Turlej-Rogacka A, Empel J, Bouchami O, Faria NA, Tavares A, Hryniewicz W, Fluit AC, de Lencastre H; CONCORD Working Group. High genetic diversity among community-associated *Staphylococcus aureus* in Europe: results from a multicenter study. PLoS One. 2012; 7: e34768.

Rosenbach FJ. Microorganismen bei den Wund-Infections-Krankheiten des Menschen. J.F. Bergmann, Wiesbaden, 1884; 1-122.

Ross JI, Eady EA, Cove JH, Cunliffe WJ, Baumberg S, Wootton JC. Inducible erythromycin resistance in staphylococci is encoded by a member of the ATP-binding transport super-gene family. Mol Microbiol. 1990; 4: 1207-1214.

Ross JE, Farrell DJ, Mendes RE, Sader HS, Jones RN. Eight-year (2002-2009) summary of the linezolid (Zyvox® Annual Appraisal of Potency and Spectrum; ZAAPS) program in European countries. J Chemother. 2011; 23: 71-76.

Rossney AS, Shore AC, Morgan PM, Fitzgibbon MM, O'Connell B, Coleman DC. The emergence and importation of diverse genotypes of methicillin-resistant *Staphylococcus aureus* (MRSA) harboring the Panton-Valentine leukocidin gene (PVL) reveal that PVL is a poor marker for community-acquired MRSA strains in Ireland. J Clin Microbiol. 2007; 45: 2554-2563.

Rountree PM, Freeman BM. Infections caused by a particular phage type of *Staphylococcus aureus*. Med J Aust. 1955; 42: 157-161.

Rountree PM, Beard MA. Hospital strains of *Staphylococcus aureus*, with particular reference to methicillin-resistant strains. Med J Aust. 1968; 2: 1163-1168.

Ruhe J, Menon A, Mushatt D, Dejace P, Hasbun R. Non- *epidermidis* coagulase-negative staphylococcal bacteremia: clinical predictors of true bacteremia. Eur J Clin Microbiol Infect Dis. 2004; 23: 495-498.

Ruiz de Gopegui E, Oliver A, Ramírez A, Gutiérrez O, Andreu C, Pérez JL. Epidemiological relatedness of methicillin-resistant *Staphylococcus aureus* from a tertiary hospital and a geriatric institution in Spain. Clin Microbiol Infect. 2004; 10: 339-342.

Ruiz de Gopegui E, Oliver A, Galmés MI, Hidalgo O, Pérez JL. Consolidación de un clon multirresistente de *Staphylococcus aureus* no relacionado con el clon Ibérico en un hospital de Mallorca. Enferm Infecc Microbiol Clin. 2005; 23: 140-144.

Ruiz de Gopegui E, Oliver A, Herrero J, Pérez JL. Neumonía nosocomial por *Staphylococcus aureus* resistente a meticilina de origen comunitario productor de leucocidina de Panton-Valentine. Enferm Infecc Microbiol Clin. 2008; 26: 533-534.

Ruiz de Gopegui E, Oliver A, Pérez JL. Epidemiología molecular de *Staphylococcus aureus* resistentes a la meticilina en un hospital de Mallorca. XIII Reunión de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC). Sevilla, 3-5 de junio de 2009. Comunicación 222.

Ruiz de Gopegui E, Marinescu CI, Díaz P, Socías A, Garau M, Ayestarán JI, Pareja A, Gallegos MC, Pérez JL, Oliver A. Diseminación nosocomial de *Staphylococcus hominis* resistente al linezolid en dos hospitales de Mallorca. Enferm Infecc Microbiol Clin. 2011; 29: 339-344.

Ruiz de Gopegui E, Juan C, Zamorano L, Pérez JL, Oliver A. Transferable multidrug resistance plasmid carrying *cfr* associated with *tet*(L), *ant(4')-Ia*, and *dfrK* genes from a clinical methicillin-resistant *Staphylococcus aureus* ST125 strain. Antimicrob Agents Chemother. 2012; 56: 2139-2142.

Ryffel C, Bucher R, Kayser FH, Berger-Bächi B. The *Staphylococcus aureus mec* determinant comprises an unusual cluster of direct repeats and codes for a gene product similar to the *Escherichia coli* Sn-glycerophosphoryl diester phosphodiesterase. J Bacteriol. 1991; 173: 7416-7422.

Sá-Leão R, Santos Sanches I, Dias D, Peres I, Barros RM, de Lencastre H. Detection of an archaic clone of *Staphylococcus aureus* with low-level resistance to methicillin in a pediatric hospital in Portugal and in international samples: relics of a formerly widely disseminated strain? J Clin Microbiol. 1999; 37: 1913-1920.

Sader HS, Rhomberg PR, Jones RN. Nine-hospital study comparing broth microdilution and Etest method results for vancomycin and daptomycin against methicillin-resistant *Staphylococcus aureus*. Antimicrob Agents Chemother. 2009; 53: 3162-3165.

Salvatierra E, Mariscal L, Céspedes V, González C, Castellano E, Nogueira JM. Evaluación de un programa de cribado de SAMR en un hospital de crónicos y larga estancia (HACLE). XVIII Congreso Nacional de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC). Valencia, 9-11 abril 2014. Comunicación nº 076.

Sambrook J, Russell DW. Preparation and transformation of competent *E. coli* using calcium chloride. CSH Protoc. 2006.

Sanches IS, Ramírez M, Troni H, Abecassis M, Padua M, Tomasz A, de Lencastre H. Evidence for the geographic spread of a methicillin-resistant *Staphylococcus aureus* clone between Portugal and Spain. J Clin Microbiol. 1995; 33: 1243-1246.

Sánchez García M, De la Torre MA, Morales G, Peláez B, Tolón MJ, Domingo S, Candel FJ, Andrade R, Arribi A, García N, Martínez Sagasti F, Fereres J, Picazo J. Clinical outbreak of linezolid-resistant *Staphylococcus aureus* in an intensive care unit. JAMA. 2010; 303: 2260-2264.

Sanchini A, Spitoni MG, Monaco M, Raglio A, Grigis A, Petrò W, Menchini M, Pesenti A, Goglio A, Pantosti A. Outbreak of skin and soft tissue infections in a hospital newborn nursery in Italy due to community-acquired meticillin-resistant *Staphylococcus aureus* USA300 clone. J Hosp Infect. 2013; 83: 36-40.

Saravolatz LD, Markowitz N, Arking L, Pohlod D, Fisher E. Methicillin-resistant *Staphylococcus aureus*. Epidemiologic observations during a community-acquired outbreak. Ann Intern Med. 1982; 96: 11-16.

Schleifer KH. Gram-positive cocci. En: Holt JG, Sneath PHA, Mair NS, Sharpe MS (ed.). Bergey's Manual of Systematic Bacteriology. Baltimore: Williams & Wilkins, 1986; 999-1002.

Schmitz FJ, Fluit AC, Gondolf M, Beyrau R, Lindenlauf E, Verhoef J, Heinz HP, Jones ME. The prevalence of aminoglycoside resistance and corresponding resistance genes in clinical

isolates of staphylococci from 19 European hospitals. J Antimicrob Chemother. 1999; 43: 253-259.

Schmitz FJ, Krey A, Sadurski R, Verhoef J, Milatovic D, Fluit AC; European SENTRY Participants. Resistance to tetracycline and distribution of tetracycline resistance genes in European *Staphylococcus aureus* isolates. J Antimicrob Chemother. 2001; 47: 239-240.

Schwarz S, Cardoso M, Wegener HC. Nucleotide sequence and phylogeny of the *tet*(L) tetracycline resistance determinant encoded by plasmid pSTE1 from *Staphylococcus hyicus*. Antimicrob Agents Chemother. 1992; 36: 580-588.

Schwarz S, Gregory PD, Werckenthin C, Curnock S, Dyke KG. A novel plasmid from *Staphylococcus epidermidis* specifying resistance to kanamycin, neomycin and tetracycline. J Med Microbiol. 1996; 45: 57-63.

Schwarz S, Werckenthin C, Kehrenberg C. Identification of a plasmid-borne chloramphenicol-florfenicol resistance gene in *Staphylococcus sciuri*. Antimicrob Agents Chemother. 2000; 44: 2530-2533.

Schwarz S, Kadlec K, Strommenger B. Methicillin-resistant *Staphylococcus aureus* and *Staphylococcus pseudintermedius* detected in the BfT-GermVet monitoring programme 2004-2006 in Germany. J Antimicrob Chemother. 2008; 61: 282-285.

Schwarzkopf A, Karch H, Schmidt H, Lenz W, Heesemann J. Phenotypical and genotypical characterization of epidemic clumping factor-negative, oxacillin-resistant *Staphylococcus aureus*. J Clin Microbiol. 1993; 31: 2281-2285.

Seral C, Sáenz Y, Algarate S, Durán E, Luque P, Torres C, Castillo FJ. Nosocomial outbreak of methicillin- and linezolid-resistant *Staphylococcus epidermidis* associated with catheter-related infections in intensive care unit patients. Int J Med Microbiol. 2011; 301: 354-358.

Sewell DL, Potter SA, Jacobson CM, Strausbaugh LJ, Ward TT. Sensitivity of surveillance cultures for the detection of methicillin-resistant *Staphylococcus aureus* in a nursing-home-care unit. Diagn Microbiol Infect Dis. 1993; 17: 53-56.

Seybold U, Kourbatova EV, Johnson JG, Halvosa SJ, Wang YF, King MD, Ray SM, Blumberg HM. Emergence of community-associated methicillin-resistant *Staphylococcus aureus* USA300 genotype as a major cause of health care-associated blood stream infections. Clin Infect Dis. 2006; 42: 647-656.

Shaw KJ, Barbachyn MR. The oxazolidinones: past, present, and future. Ann N Y Acad Sci. 2011; 1241: 48-70.

Shen J, Wang Y, Schwarz S. Presence and dissemination of the multiresistance gene *cfr* in Gram-positive and Gram-negative bacteria. J Antimicrob Chemother. 2013; 68: 1697-1706.

Shenoy ES, Paras ML, Noubary F, Walensky RP, Hooper DC. Natural history of colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE): a systematic review. BMC Infect Dis. 2014; 14: 177.

Shishido K, Tanaka Y. A restriction map of *Bacillus subtilis* tetracycline-resistance plasmid pNS1981. Plasmid. 1984; 12: 65-66.

Shore AC, Brennan OM, Ehricht R, Monecke S, Schwarz S, Slickers P, Coleman DC. Identification and characterization of the multidrug resistance gene *cfr* in a Panton-Valentine leukocidin-positive sequence type 8 methicillin-resistant *Staphylococcus aureus* IVa (USA300) isolate. Antimicrob Agents Chemother. 2010a; 54: 4978-4984.

Shore AC, Rossney AS, Kinnevey PM, Brennan OM, Creamer E, Sherlock O, Dolan A, Cunney R, Sullivan DJ, Goering RV, Humphreys H, Coleman DC. Enhanced discrimination of highly clonal ST22-methicillin-resistant *Staphylococcus aureus* IV isolates achieved by combining *spa*, *dru*, and pulsed-field gel electrophoresis typing data. J Clin Microbiol. 2010b; 48: 1839-1852.

Shore AC, Deasy EC, Slickers P, Brennan G, O'Connell B, Monecke S, Ehricht R, Coleman DC. Detection of staphylococcal cassette chromosome *mec* type XI carrying highly divergent *mecA*, *mecI*, *mecR1*, *blaZ*, and *ccr* genes in human clinical isolates of clonal complex 130 methicillin-resistant *Staphylococcus aureus*. Antimicrob Agents Chemother. 2011; 55: 3765-3773.

Shore AC, Brennan OM, Deasy EC, Rossney AS, Kinnevey PM, Ehricht R, Monecke S, Coleman DC. DNA microarray profiling of a diverse collection of nosocomial methicillin-resistant *Staphylococcus aureus* isolates assigns the majority to the correct sequence type and staphylococcal cassette chromosome *mec* (SCC*mec*) type and results in the subsequent identification and characterization of novel SCC*mec*-SCCM1 composite islands. Antimicrob Agents Chemother. 2012; 56: 5340-5355.

Sierra JM, Camoez M, Tubau F, Gasch O, Pujol M, Martín R, Domínguez MA. Low prevalence of c*fr*-mediated linezolid resistance among methicillin-resistant *Staphylococcus aureus* in a Spanish hospital: case report on linezolid resistance acquired during linezolid therapy. PLoS One. 2013; 8: e59215.

Singh A, Goering RV, Simjee S, Foley SL, Zervos MJ. Application of molecular techniques to the study of hospital infection. Clin Microbiol Rev. 2006; 19: 512-530.

Sivapalasingam S, Steigbigel, NH. Macrólidos, clindamicina y cetólidos. En: Mandell GL, Bennett JE, Dolin R (ed.). Enfermedades Infecciosas, Principios y Práctica. 7ª ed. Barcelona: Elsevier, 2012; 427-449.

Skinner D, Keefer CS. Significance of bacteremia caused by *Staphylococcus aureus*. Arch Intern Med. 1941; 68: 851-875.

Smith JM, Cook GM. A decade of community MRSA in New Zealand. Epidemiol Infect. 2005; 133: 899-904.

Smith LK, Mankin AS. Transcriptional and translational control of the *mlr* operon, which confers resistance to seven classes of protein synthesis inhibitors. Antimicrob Agents Chemother. 2008a; 52: 1703-1712.

Smith CS, Parnell P, Hodgson G, Darby B, Barr B, Tompkins D, Heritage J, Wilcox MH. Are methicillin-resistant *Staphylococcus aureus* that produce Panton-Valentine leucocidin (PVL) found among residents of care homes? J Antimicrob Chemother. 2008b; 62: 968-972.

Sobral D, Schwarz S, Bergonier D, Brisabois A, Feßler AT, Gilbert FB, Kadlec K, Lebeau B, Loisy-Hamon F, Treilles M, Pourcel C, Vergnaud G. High throughput multiple locus variable number of tandem repeat analysis (MLVA) of *Staphylococcus aureus* from human, animal and food sources. PLoS One. 2012; 7: e33967.

Solberg CO. A study of carriers of *Staphylococcus aureus* with special regard to quantitative bacterial estimations. Acta Med Scand 1965; 436 (Suppl): 1-96.

Sompolinsky D, Samra Z, Karakawa WW, Vann WF, Schneerson R, Malik Z. Encapsulation and capsular types in isolates of *Staphylococcus aureus* from different sources and relationship to phage types. J Clin Microbiol. 1985; 22: 828-834.

Song MD, Wachi M, Doi M, Ishino F, Matsuhashi M. Evolution of an inducible penicillin-target protein in methicillin-resistant *Staphylococcus aureus* by gene fusion. FEBS Lett. 1987; 221: 167-171.

Soriano A, Marco F, Martínez JA, Pisos E, Almela M, Dimova VP, Álamo D, Ortega M, López J, Mensa J. Influence of vancomycin minimum inhibitory concentration on the treatment of methicillin-resistant *Staphylococcus aureus* bacteremia. Clin Infect Dis. 2008; 46: 193-200.

Sorlozano A, Gutiérrez J, Martínez T, Yuste ME, Pérez-López JA, Vindel A, Guillén J, Boquete T. Detection of new mutations conferring resistance to linezolid in glycopeptide-intermediate susceptibility *Staphylococcus hominis* subspecies *hominis* circulating in an intensive care unit. Eur J Clin Microbiol Infect Dis. 2010; 29: 73-80.

Spaan AN, Henry T, van Rooijen WJ, Perret M, Badiou C, Aerts PC, Kemmink J, de Haas CJ, van Kessel KP, Vandenesch F, Lina G, van Strijp JA. The staphylococcal toxin Panton-Valentine Leukocidin targets human C5a receptors. Cell Host Microbe. 2013; 13: 584-594.

Squeri R, Grillo OC, La Fauci V. Surveillance and evidence of contamination in hospital environment from meticillin and vancomycin-resistant microbial agents. J Prev Med Hyg. 2012; 53: 143-145.

Stefani S, Chung DR, Lindsay JA, Friedrich AW, Kearns AM, Westh H, Mackenzie FM. Meticillin-resistant *Staphylococcus aureus* (MRSA): global epidemiology and harmonisation of typing methods. Int J Antimicrob Agents. 2012; 39: 273-282.

Stewart GT, Holt RJ. Evolution of natural resistance to the newer penicillins. Br Med J. 1963; 1: 308-311.

Stone ND, Lewis DR, Lowery HK, Darrow LA, Kroll CM, Gaynes RP, Jernigan JA, McGowan JE Jr, Tenover FC, Richards CL Jr. Importance of bacterial burden among methicillin-resistant *Staphylococcus aureus* carriers in a long-term care facility. Infect Control Hosp Epidemiol. 2008; 29: 143-148.

Stone ND, Lewis DR, Johnson TM 2nd, Hartney T, Chandler D, Byrd-Sellers J, McGowan JE Jr, Tenover FC, Jernigan JA, Gaynes RP; Southeast Veterans Affairs Long-Term Care Methicillin-Resistant *Staphylococcus aureus* Cooperative. Methicillin-resistant *Staphylococcus aureus* (MRSA) nasal carriage in residents of Veterans Affairs long-term care facilities: role of antimicrobial exposure and MRSA acquisition. Infect Control Hosp Epidemiol. 2012; 33: 551-557.

Strommenger B, Braulke C, Heuck D, Schmidt C, Pasemann B, Nübel U, Witte W. *spa* typing of *Staphylococcus aureus* as a frontline tool in epidemiological typing. J Clin Microbiol. 2008; 46: 574-581.

Strommenger B, Bartels MD, Kurt K, Layer F, Rohde SM, Boye K, Westh H, Witte W, De Lencastre H, Nübel U. Evolution of methicillin-resistant *Staphylococcus aureus* towards increasing resistance. J Antimicrob Chemother. 2014; 69: 616-622.

Sunbul M, Demirag MK, Yilmaz O, Yilmaz H, Ozturk R, Leblebicioglu H. Pacemaker lead endocarditis caused by *Staphylococcus hominis*. Pacing Clin Electrophysiol. 2006; 29: 543-545.

Swaney SM, Aoki H, Ganoza MC, Shinabarger DL. The oxazolidinone linezolid inhibits initiation of protein synthesis in bacteria. Antimicrob Agents Chemother. 1998; 42: 3251-3255.

Talon DR, Bertrand X. Methicillin-resistant *Staphylococcus aureus* in geriatric patients: usefulness of screening in a chronic-care setting. Infect Control Hosp Epidemiol. 2001; 22: 505-509.

Tenover FC, Arbeit RD, Goering RV, Mickelsen PA, Murray BE, Persing DH, Swaminathan B. Interpreting chromosomal DNA restriction patterns produced by pulsed-field gel electrophoresis: criteria for bacterial strain typing. J Clin Microbiol. 1995; 33: 2233-2239.

Tenover FC. Community-associated methicillin resistant *Staphylococcus aureus*: It's not just in communities anymore. Clin Microbiol Newsletter. 2006; 28: 33-36.

Tenover FC, Goering RV. Methicillin-resistant *Staphylococcus aureus* strain USA300: origin and epidemiology. J Antimicrob Chemother. 2009; 64: 441-446.

Terpenning MS, Bradley SF, Wan JY, Chenoweth CE, Jorgensen KA, Kauffman CA. Colonization and infection with antibiotic-resistant bacteria in a long-term care facility. J Am Geriatr Soc. 1994; 42: 1062-1069.

Toh SM, Xiong L, Arias CA, Villegas MV, Lolans K, Quinn J, Mankin AS. Acquisition of a natural resistance gene renders a clinical strain of methicillin-resistant *Staphylococcus aureus* resistant to the synthetic antibiotic linezolid. Mol Microbiol. 2007; 64: 1506-1514.

Tortora GL, Funke BR, Case CL. Genética microbiana. En: Tortora GL, Funke BR, Case CL. Introducción a la Microbiología. 9ª ed. Buenos Aires: Editorial Médica Panamericana, 2007; 225-227.

Treviño M, Martínez-Lamas L, Romero-Jung PA, Giráldez JM, Alvarez-Escudero J, Regueiro BJ. Endemic linezolid-resistant *Staphylococcus epidermidis* in a critical care unit. Eur J Clin Microbiol Infect Dis. 2009; 28: 527-533.

Tsakris A, Pillai SK, Gold HS, Thauvin-Eliopoulos C, Venkataraman L, Wennersten C, Moellering RC Jr, Eliopoulos GM. Persistence of rRNA operon mutated copies and rapid re-emergence of linezolid resistance in *Staphylococcus aureus*. Antimicrob Chemother. 2007; 60: 649-651.

Tsiodras S, Gold HS, Sakoulas G, Eliopoulos GM, Wennersten C, Venkataraman L, Moellering RC, Ferraro MJ. Linezolid resistance in a clinical isolate of *Staphylococcus aureus*. Lancet. 2001; 358: 207-208.

Tsubakishita S, Kuwahara-Arai K, Sasaki T, Hiramatsu K. Origin and molecular evolution of the determinant of methicillin resistance in staphylococci. Antimicrob Agents Chemother. 2010; 54: 4352-4359.

Turlej A, Hryniewicz W, Empel J. Staphylococcal cassette chromosome *mec* (SCC*mec*) classification and typing methods: an overview. Pol J Microbiol. 2011; 60: 95-103.

Udo EE, Pearman JW, Grubb WB. Genetic analysis of community isolates of methicillin-resistant *Staphylococcus aureus* in Western Australia. J Hosp Infect. 1993; 25: 97-108.

van Belkum A, van Leeuwen W, Kaufmann ME, Cookson B, Forey F, Etienne J, Goering R, Tenover F, Steward C, O'Brien F, Grubb W, Tassios P, Legakis N, Morvan A, El Solh N, de Ryck R, Struelens M, Salmenlinna S, Vuopio-Varkila J, Kooistra M, Talens A, Witte W, Verbrugh H. Assessment of resolution and intercenter reproducibility of results of genotyping

Staphylococcus aureus by pulsed-field gel electrophoresis of *Sma*I macrorestriction fragments: a multicenter study. J Clin Microbiol. 1998; 36: 1653-1659.

van Belkum A, Verkaik NJ, de Vogel CP, Boelens HA, Verveer J, Nouwen JL, Verbrugh HA, Wertheim HF. Reclassification of *Staphylococcus aureus* nasal carriage types. J Infect Dis. 2009; 199: 1820-1826.

van Cleef BA, Monnet DL, Voss A, Krziwanek K, Allerberger F, Struelens M, Zemlickova H, Skov RL, Vuopio-Varkila J, Cuny C, Friedrich AW, Spiliopoulou I, Pászti J, Hardardottir H, Rossney A, Pan A, Pantosti A, Borg M, Grundmann H, Mueller-Premru M, Olsson-Liljequist B, Widmer A, Harbarth S, Schweiger A, Unal S, Kluytmans JA. Livestock-associated methicillin-resistant *Staphylococcus aureus* in humans, Europe. Emerg Infect Dis. 2011; 17: 502-505.

van den Broek IV, Van Cleef BA, Haenen A, Broens EM, van der Wolf PJ, van den Broek MJ, Huijsdens XW, Kluytmans JA, van de Giessen AW, Tiemersma EW. Methicillin-resistant *Staphylococcus aureus* in people living and working in pig farms. Epidemiol Infect. 2009; 137: 700-708.

van de Velde H. Étude sur la mécanisme de la virulence du staphylocoque pyogène. Cellule. 1894; 10: 402–460.

VandenBergh MF, Yzerman EP, van Belkum A, Boelens HA, Sijmons M, Verbrugh HA. Follow-up of *Staphylococcus aureus* nasal carriage after 8 years: redefining the persistent carrier state. J Clin Microbiol. 1999; 37: 3133-3340.

van Gils EJ, Hak E, Veenhoven RH, Rodenburg GD, Bogaert D, Bruin JP, van Alphen L, Sanders EA. Effect of seven-valent pneumococcal conjugate vaccine on *Staphylococcus aureus* colonisation in a randomised controlled trial. PLoS One. 2011; 6: e20229.

van Hal SJ, Lodise TP, Paterson DL. The clinical significance of vancomycin minimum inhibitory concentration in *Staphylococcus aureus* infections: a systematic review and meta-analysis. Clin Infect Dis. 2012; 54: 755-771.

Vanhoof R, Godard C, Content J, Nyssen HJ, Hannecart-Pokorni E. Detection by polymerase chain reaction of genes encoding aminoglycoside-modifying enzymes in methicillin-resistant *Staphylococcus aureus* isolates of epidemic phage types. Belgian Study Group of Hospital Infections (GDEPIH/GOSPIZ). J Med Microbiol. 1994; 41: 282-290.

van Loo IH, van Dijk S, Verbakel-Schelle I, Buiting AG. Evaluation of a chromogenic agar (MRSASelect) for the detection of meticillin-resistant *Staphylococcus aureus* with clinical samples in The Netherlands. J Med Microbiol. 2007; 56: 491-494.

Verhoeven PO, Grattard F, Carricajo A, Lucht F, Cazorla C, Garraud O, Pozzetto B, Berthelot P. An algorithm based on one or two nasal samples is accurate to identify persistent nasal carriers of *Staphylococcus aureus*. Clin Microbiol Infect. 2012; 18: 551-557.

Verhoeven PO, Gagnaire J, Botelho-Nevers E, Grattard F, Carricajo A, Lucht F, Pozzetto B, Berthelot P. Detection and clinical relevance of *Staphylococcus aureus* nasal carriage: an update. Expert Rev Anti Infect Ther. 2014; 12: 75-89.

Versalovic J, Koeuth T, Lupski JR. Distribution of repetitive DNA sequences in eubacteria and application to fingerprinting of bacterial genomes. Nucleic Acids Res. 1991; 19: 6823-6831.

Vindel A, Trincado P, Gómez E, Cabrera R, Boquete T, Solá C, Valdezate S, Saez-Nieto JA. Prevalence and evolution of methicillin-resistant *Staphylococcus aureus* in Spanish hospitals between 1996 and 2002. J Clin Microbiol. 2006; 44: 266-270.

Vindel A, Cuevas O, Cercenado E, Marcos C, Bautista V, Castellares C, Trincado P, Boquete T, Pérez-Vázquez M, Marín M, Bouza E; Spanish Group for the Study of *Staphylococcus*. Methicillin-resistant *Staphylococcus aureus* in Spain: molecular epidemiology and utility of different typing methods. J Clin Microbiol. 2009; 47: 1620-1627.

Vindel A, Trincado P, Cuevas O, Ballesteros C, Bouza E, Cercenado E. Molecular epidemiology of community-associated methicillin-resistant *Staphylococcus aureus* in Spain: 2004-12. J Antimicrob Chemother. 2014; 69: 2913-2919.

von Baum H, Schmidt C, Svoboda D, Bock-Hensley O, Wendt C. Risk factors for methicillin-resistant *Staphylococcus aureus* carriage in residents of German nursing homes. Infect Control Hosp Epidemiol. 2002; 23: 511-515.

von Eiff C, Becker K, Machka K, Stammer H, Peters G. Nasal carriage as a source of *Staphylococcus aureus* bacteremia. Study Group. N Engl J Med. 2001; 344: 11-16.

Voyich JM, Otto M, Mathema B, Braughton KR, Whitney AR, Welty D, Long RD, Dorward DW, Gardner DJ, Lina G, Kreiswirth BN, DeLeo FR. Is Panton-Valentine leukocidin the major virulence determinant in community-associated methicillin-resistant *Staphylococcus aureus* disease? J Infect Dis. 2006; 194: 1761-1770.

Wang SC, Frey PA. S-adenosylmethionine as an oxidant: the radical SAM superfamily. Trends Biochem Sci. 2007; 32: 101-110.

Wang Y, Wang Y, Wu CM, Schwarz S, Shen Z, Zhang W, Zhang Q, Shen JZ. Detection of the staphylococcal multiresistance gene *cfr* in *Proteus vulgaris* of food animal origin. J Antimicrob Chemother. 2011; 66: 2521-2526.

Wang Y, He T, Schwarz S, Zhou D, Shen Z, Wu C, Wang Y, Ma L, Zhang Q, Shen J. Detection of the staphylococcal multiresistance gene *cfr* in *Escherichia coli* of domestic-animal origin. J Antimicrob Chemother. 2012a; 67: 1094-1098.

Wang Y, Schwarz S, Shen Z, Zhou N, Lin J, Wu C, Shen J. Detection of the staphylococcal multiresistance gene *cfr* in *Macrococcus caseolyticus* and *Jeotgalicoccus pinnipedialis*. J Antimicrob Chemother. 2012b; 67: 1824-1827.

Wang Y, Zhang W, Wang J, Wu C, Shen Z, Fu X, Yan Y, Zhang Q, Schwarz S, Shen J. Distribution of the multidrug resistance gene *cfr* in *Staphylococcus* species isolates from swine farms in China. Antimicrob Agents Chemother. 2012c; 56: 1485-1490.

Wannet WJ, Spalburg E, Heck ME, Pluister GN, Tiemersma E, Willems RJ, Huijsdens XW, de Neeling AJ, Etienne J. Emergence of virulent methicillin-resistant *Staphylococcus aureus* strains carrying Panton-Valentine leucocidin genes in The Netherlands. J Clin Microbiol. 2005; 43: 3341-3345.

Watkins RR, David MZ, Salata RA. Current concepts on the virulence mechanisms of meticillin-resistant *Staphylococcus aureus*. J Med Microbiol. 2012; 61: 1179-1193.

Weiß S, Kadlec K, Feßler AT, Schwarz S. Complete sequence of a multiresistance plasmid from a methicillin-resistant *Staphylococcus epidermidis* ST5 isolated in a small animal clinic. J Antimicrob Chemother. 2014; 69: 847-859.

Weidenmaier C, Kokai-Kun JF, Kristian SA, Chanturiya T, Kalbacher H, Gross M, Nicholson G, Neumeister B, Mond JJ, Peschel A. Role of teichoic acids in *Staphylococcus aureus* nasal colonization, a major risk factor in nosocomial infections. Nat Med. 2004; 10: 243-245.

Werckenthin C, Schwarz S, Roberts MC. Integration of pT181-like tetracycline resistance plasmids into large staphylococcal plasmids involves IS*257*. Antimicrob Agents Chemother. 1996; 40: 2542-2544.

Wertheim HF, Melles DC, Vos MC, van Leeuwen W, van Belkum A, Verbrugh HA, Nouwen JL. The role of nasal carriage in *Staphylococcus aureus* infections. Lancet Infect Dis. 2005; 5: 751-762.

Wertheim HF, van Kleef M, Vos MC, Ott A, Verbrugh HA, Fokkens W. Nose picking and nasal carriage of *Staphylococcus aureus*. Infect Control Hosp Epidemiol. 2006; 27: 863-867.

Wielders CL, Vriens MR, Brisse S, de Graaf-Miltenburg LA, Troelstra A, Fleer A, Schmitz FJ, Verhoef J, Fluit AC. In-vivo transfer of *mecA* DNA to *Staphylococcus aureus* [corrected]. Lancet. 2001; 357: 1674-1675.

Williams REO. Healthy carriage of *Staphylococcus aureus*: its prevalence and importance. Bacteriol Rev. 1963; 26**:** 56–71.

Wilson P, Andrews JA, Charlesworth R, Walesby R, Singer M, Farrell DJ, Robbins M. Linezolid resistance in clinical isolates of *Staphylococcus aureus*. J Antimicrob Chemother. 2003; 51: 186-188.

Wilson DN, Schluenzen F, Harms JM, Starosta AL, Connell SR, Fucini P. The oxazolidinone antibiotics perturb the ribosomal peptidyl-transferase center and effect tRNA positioning. Proc Natl Acad Sci USA. 2008; 105: 13339-13344.

Wilson R, Sethi S, Anzueto A, Miravitlles M. Antibiotics for treatment and prevention of exacerbations of chronic obstructive pulmonary disease. J Infect. 2013; 67: 497-515.

Wisplinghoff H, Rosato AE, Enright MC, Noto M, Craig W, Archer GL. Related clones containing SCC*mec* type IV predominate among clinically significant *Staphylococcus epidermidis* isolates. Antimicrob Agents Chemother. 2003; 47: 3574-3579.

Wisplinghoff H, Ewertz B, Wisplinghoff S, Stefanik D, Plum G, Perdreau-Remington F, Seifert H. Molecular evolution of methicillin-resistant *Staphylococcus aureus* in the metropolitan area of Cologne, Germany, from 1984 to 1998. J Clin Microbiol. 2005; 43: 5445-5451.

Witte W, Cuny C, Braulke C, Heuck D. Clonal dissemination of two MRSA strains in Germany. Epidemiol Infect. 1994; 113: 67-73.

Witte W. Antibiotic resistance in gram-positive bacteria: epidemiological aspects. J Antimicrob Chemother. 1999; 44 (Suppl A): 1-9.

Witte W, Enright M, Schmitz FJ, Cuny C, Braulke C, Heuck D. Characteristics of a new epidemic MRSA in Germany ancestral to United Kingdom EMRSA 15. Int J Med Microbiol. 2001; 290: 677-682.

Witte W, Cuny C. Emergence and spread of *cfr*-mediated multiresistance in staphylococci: an interdisciplinary challenge. Future Microbiol. 2011; 6: 925-931.

Woltering R, Hoffmann G, Daniels-Haardt I, Gastmeier P, Chaberny IF. Prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in patients in long-term care in hospitals, rehabilitation centers and nursing homes of a rural district in Germany. Dtsch Med Wochenschr. 2008; 133: 999-1003.

Woodford N, Livermore DM. Infections caused by Gram-positive bacteria: a review of the global challenge. J Infect. 2009; 59 (Suppl 1): S4-16.

Wu S, Piscitelli C, de Lencastre H, Tomasz A. Tracking the evolutionary origin of the methicillin resistance gene: cloning and sequencing of a homologue of *mecA* from a methicillin susceptible strain of *Staphylococcus sciuri*. Microb Drug Resist. 1996; 2: 435-441.

Yao JDC, Moellerig RC, Jr. Antibacterial agents. En: Versalovic J, Carroll KC, Funke G, Jorgensen JH, Landry ML, Warnock DW (ed.). Manual of Clinical Microbiology. 10ª ed. Washington, DC: ASM Press, 2011; 1043-1081.

Yoshida K, Shoji H, Hanaki H, Yanagisawa C, Ikeda-Dantsuji Y, Fukuchi K, Adachi M, Niki Y. Linezolid-resistant methicillin-resistant *Staphylococcus aureus* isolated after long-term, repeated use of linezolid. J Infect Chemother. 2009; 15: 417-419.

Yu VL, Goetz A, Wagener M, Smith PB, Rihs JD, Hanchett J, Zuravleff JJ. *Staphylococcus aureus* nasal carriage and infection in patients on hemodialysis. Efficacy of antibiotic prophylaxis. N Engl J Med. 1986; 315: 91-96.

Zhang K, McClure JA, Elsayed S, Louie T, Conly JM. Novel multiplex PCR assay for characterization and concomitant subtyping of staphylococcal cassette chromosome *mec* types I to V in methicillin-resistant *Staphylococcus aureus*. J Clin Microbiol. 2005; 43: 5026-5033.

Zhang L, Thomas JC, Miragaia M, Bouchami O, Chaves F, d'Azevedo PA, Aanensen DM, de Lencastre H, Gray BM, Robinson DA. Multilocus sequence typing and further genetic characterization of the enigmatic pathogen, *Staphylococcus hominis*. PLoS One. 2013; 8: e66496.

Zhu W, Tenover FC, Limor J, Lonsway D, Prince D, Dunne WM Jr, Patel JB. Use of pyrosequencing to identify point mutations in domain V of 23S rRNA genes of linezolid-resistant *Staphylococcus aureus* and *Staphylococcus epidermidis*. Eur J Clin Microbiol Infect Dis. 2007; 26: 161-165.

Zong Z, Lü X. Characterization of a new SCC*mec* element in *Staphylococcus cohnii*. PLoS One. 2010; 5: e14016.

Zurenko GE, Yagi BH, Schaadt RD, Allison JW, Kilburn JO, Glickman SE, Hutchinson DK, Barbachyn MR, Brickner SJ. In vitro activities of U-100592 and U-100766, novel oxazolidinone antibacterial agents. Antimicrob Agents Chemother. 1996; 40: 839-845.

Zurenko GE, Todd WM, Hafkin BA. Development of linezolid-resistant *Enterococcus faecium* in two compassionate use program patients treated with linezolid. Proceedings of the 39th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC); San Francisco, EEUU; 26–29 septiembre de 1999.