Travel of microbial resistance in a global perspective:

Community-acquired MRSA

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Gazi University Medical School

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Methicillin-Resistant Staphylococcus aureus (MRSA)

- ✓ 1970 epidemics in healthcare settings
  - leading to endemnicity
- ✓ Healthcare Associated MRSA (HCA-MRSA)
  - Generally resistant to most antibiotics
- ✓ Known Risk factors for HCA-MRSA
  - prolonged hospitalization
  - care in an intensive care unit
  - prolonged antimicrobial therapy

Dietrich DW, et al. Pediatrics 2004;113:347-352.
Salgado CD, et al. CID 2003;36:131-9.
Elston JWT, Barlow GT. J Infect 2009; 59: 149-155

Community-Acquired Methicillin-Resistant Staphylococcus aureus (CA-MRSA)

- ✓ A new strain of MRSA
  - presenting from the community
  - in persons without traditional risk factors for MRSA
- ✓ Differing from HCA-MRSA in terms of
  - Epidemiology
  - Antibiotic sensitivity patterns
  - Virulence
  - Presentation

Elston JWT, Barlow GT. J Infect 2009; 59: 149-155
Mediavilla JR, et al. Current Opinion in Microbiology 2012, 15:588–595

Proposed Theories

- ✓ Linked with the worldwide increase in fluoroquinolone use
- ✓ Vacant colonization niches following global immunization efforts against S. pneumoniae
- ✓ Potential role of PVL in the origin and dissemination of CA-MRSA
- ✓ Appearance of SCCmec type IV during the late 1980s presumably driving the simultaneous emergence of multiple CA-MRSA lineages
- ✓ Distinct PVL+ MSSA lineages subsequently acquiring SCCmec IV or V elements

Begier E,et al. CID 2004;39:1446-53.
Carleton HA, et al. JID 2004;190:1730-8.
Tirabassi MV, et al. J Ped Surg 2005;40:962-966

No single explanation:
Classic Triad of Host, Pathogen and Environment

- ✓ Emergence of livestock-associated MRSA strains

continuously emergent phenomenon

Zetola N, et al. Lancet 2005;5:275-86.
Fluit AC. CMI 2012; 18(8): 735-744.

CA-MRSA vs HA-MRSA

- ✓ CA-MRSA
  - Staphy. cassette chromosome(SCC) type IV
    - Small, highly mobile
    - Confers resistance ONLY to beta-lactams.
  - Replicate more rapidly

  - Surviving advantage & Greater mobility

- ✓ Carry the Panton-Valentine leukocidin (PVL) gene,
  - Codes for a leukocyte toxin

    ↳ increased virulence (?)

Elston JWT, Barlow GT. J Infect 2009; 59: 149-155

Family clusters...

Community-associated methicillin-resistant *Staphylococcus aureus* disease in two members of a household in Spain

Infección invasora por Staphylococcus aureus comunitario en dos miembros de una familia

Dear Editor:

We present 2 cases of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) pneumonia in a young, previously healthy woman and her newborn. To the best of our knowledge this is the first reported intra-family cluster of CA-MRSA pneumonia. If reported cases of household transmission of invasive CA-MRSA increase, stricter infection control measures might be needed in the management of these patients and their households.

Enferm Infecc Microbiol Clin. 2010;28(7):471–476

Journal of Medical Microbiology (2010), **59**, 489–492 DOI 10.1099/jmm.0.015925-0

Case Report

Spread of community-acquired meticillin-resistant *Staphylococcus aureus* skin and soft-tissue infection within a family: implications for antibiotic therapy and prevention

N. H. Amir,[1] A. S. Rossney,[2] J. Veale,[3] M. O'Connor,[1] F. Fitzpatrick[1,4] and H. Humphreys[1,5]

Molecular Typing Methods for S. aureus

- ✓ For numerous bacterial and fungal species
  - Pulsed-Field Gel Electrophoresis (PFGE)
    - USA ⟶ USA100, USA200, USA300, so on
    - United Kingdom ⟶ EMRSA
    - Western Australia ⟶ WA
    - Canada ⟶ CMRSA
  - Multilocus Sequence Typing (MLST)
    - universal nomenclature
- ✓ Specific to staphylococci
  - spa typing,
    - 10 000 unique patterns known as ‘spa types
  - SCCmec typing

Mediavilla JR, et al. Current Opinion in Microbiology 2012, 15:588–595

Origin and Emergence

- ✓ Putative CA-MRSA cases among i.v. drug users and aborigins.
  - WA-1, MW2 (CC)
- ✓ In 1999
  - a report describing four pediatric fatalities in the midwestern US
- ✓ 2000… outbreaks in athletes and prisoners
  - USA300 (CC8)
- ✓ Primary cause of SSTI in US
  - USA400

Elston JWT, Barlow GT. J Infect 2009; 59: 149-155
Mediavilla JR, et al. Current Opinion in Microbiology 2012, 15:588–595

Methicillin-Resistant *Staphylococcus aureus*, Geneva, land, 2005

arth,*[1]
ızi,*
ier Pittet,*

Conclusions

We studied 2 collections of non-multiresistant MRSA strains identified over a 13-year period at our institution. Our analysis showed that sporadic PVL-positive CA-MRSA has been isolated in Geneva since 1994; the largest cluster corresponded to ST 80 (SCC*mec* IV, PVL positive); the PVL gene is disseminated in many genetic backgrounds; strains showed diversity of genomic content; several epidemiologic clusters were identified; and many cases were linked to migration and travel.

Our data showed that resistance to fusidic acid or susceptibility to gentamicin should not be used as phenotypic criteria for CA-MRSA in Europe. For example, gentamicin-resistant ST152-MRSA-V found in 5 patients from Kosovo is common.

Emerging Infectious Diseases 2008;14 (2):304

During the same period…

- ✓ Genetically distinct CA-MRSA lineages from numerous countries,
  - Some lineages with restricted geographic ranges,
  - Some with international epidemicity

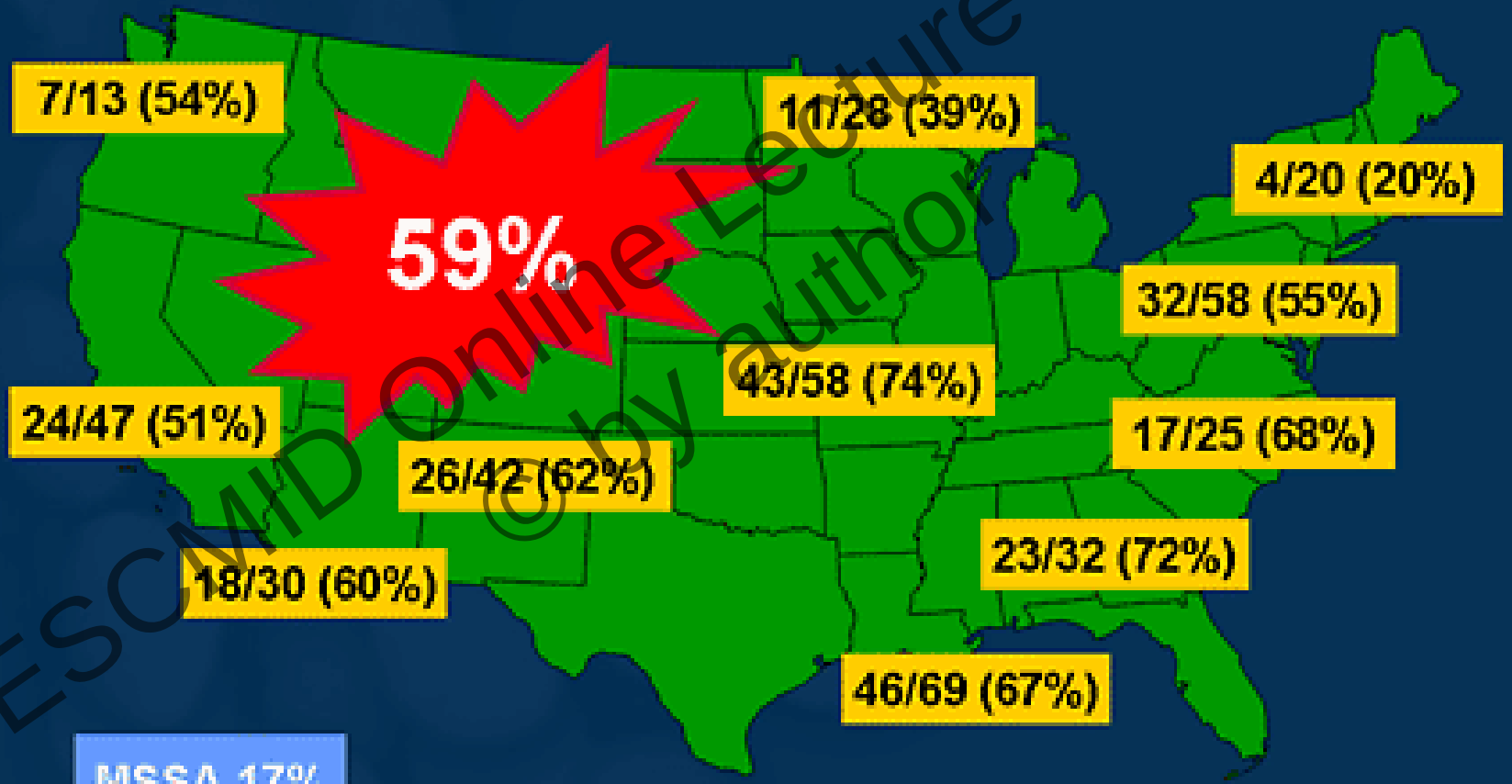
Vandenesch F, et al. Emerg Infect Dis 2003, 9:978-984.

CA-MRSA: Endemicity

- ✓ Colonization rates are generally low
- ✓ Infection rates are increasing
  - In Los Angeles, CA-MRSA was the most common cause of community-acquired SSTI presenting to emergency rooms
  - In Houston, 56% in 2000-2001, 57% in 2002 and 78% in 2003 of CA-SA in pediatrics
  - In Rhode Island, up to 40% of children with MRSA have community acquired strains

Dietrich DW, et al. Pediatrics 2004;113:347-352.
Moran GJ, et al. Emerging Infectious Diseases 2005;11:928-930.
Johnson LB, Saravolatz, LD. Infect Med. 2005;22:16-20.

Prevalence of MRSA Among 422 ED Patients With SSTI



Moran GJ et al. *Acad Emerg Med*. 2005;12(suppl 1):64.

Journal of Antimicrobial Chemotherapy (2005) **56**, 1103–1106
doi:10.1093/jac/dki379
Advance Access publication 13 October 2005

JAC

Polyclonal emergence and importation of community-acquired methicillin-resistant *Staphylococcus aureus* strains harbouring Panton-Valentine leucocidin genes in Belgium

O. Denis[1]*, A. Deplano[1], H. De Beenhouwer[2], M. Hallin[1], G. Huysmans[2], M. G. Garrino[3], Y. Glupczynski[4], X. Malaviolle[1], A. Vergison[5] and M. J. Struelens[1]

Journal of Antimicrobial Chemotherapy (2009) **63**, 21–31
doi:10.1093/jac/dkn430
Advance Access publication 23 October 2008

JAC

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*

María Pérez-Vázquez[1], Ana Vindel[2], Carmen Marcos[2], Jesús Oteo[1], Oscar Cuevas[1], Pilar Trincado[2], Verónica Bautista[1], Hajo Grundmann[3,4] and José Campos[1,5]* on behalf of the EARSS Spain *spa*-typing Group†

USA vs Europe

- ✓ Less prevalent in Europe
- ✓ Considerable genetic heterogeneity
  - European CA-MRSA' clone ST80-IV
    - İsolated in every country
- ✓ 1993 Danish reports of North African immigrants
  - In 2003 Greek reports (most prevalent)

Chua K, et al. CID 2011, 52:99-114.
Otter JA, French GL: Lancet Infect Dis 2010, 10:227-239.
Tristan A, et al. Emerg Infect Dis 2007, 13:594-600.
Mediavilla JR, et al. Current Opinion in Microbiology 2012, 15:588–595

Molecular Epidemiology

- ✓ >20 distinct genetic lineages
  - ST1-IV (WA-1, USA400)
  - **ST8-IV (USA300)**
  - **ST30-IV (South West Pacific clone)**
    - Diverged from EMRSA-16
    - Primary strains in Australia, Asia South America, Europe and Middle East
    - Serious infections /more susceptible
  - ST59-V (Taiwan clone)
  - ST80-IV (European clone)

Carleton HA, , et al. JID 2004;190:1730-8.
Mediavilla JR, et al. Current Opinion in Microbiology 2012, 15:588–595

- ✓ ST59-IV (USA1000)
  - Restricted to USA
- ✓ ST59-V
  - Taiwan and Australia
- ✓ ST1-IV
  - Native American communities (USA400)
    - Alaska
    - Midwestern regions
  - Canada (CMRSA-7)
  - Aboriginal communities (WA-1)
    - PVL (-)

Nichol KA, et al. Diagn Microbiol Infect Dis 2011, 69:320-325.
Nimmo GR, Coombs GW: Int J Antimicrob Agents 2008, 31:401-410.

ST772-V (Bengal Bay clone),

- ✓ Single locus variant of ST1
  - virulent
  - unusually resistant CA-MRSA strain
- ✓ in Bangladesh and India
- ✓ Increasingly reported in the U.K. & Europe

Shambat SM, et al.BMC Microbiol 2012, 12:64.
Brennan GI, et al. J Clin Microbiol 2012, 50:841-847.

Other clones…

- ✓ ST72-IV (USA700) ⟶ South Korea
- ✓ ST88-IV (or ST88-V) ⟶ Africa and Asia
- ✓ ST93-IV(Queensland clone) ⟶ primary str. in Australia,
- ✓ ST97-V,
  - originally of animal origin
  - recently described in the U.K.

Chua K, et al. CID 2011, 52:99-114.
Tristan A, et al. Emerg Infect Dis 2007, 13:594-600.
Kim ES, et al. J Clin Microbiol 2011, 49:1979-1982.
Breurec S, et al. Clin Microbiol Infect 2010, 17:160-165.
Ellington MJ, et al. JAC 2008, 61:73-77.

More other clones…

- ✓ ST152- V & ST377-V,
  - PVL+ methicillin-susceptible S. aureus
    - Africa
  - CA-MRSA
    - Balkans & central Europe
- ✓ ST75-IV
  - a potential subspecies
  - restricted to remote aboriginal communities

Table 1

Genotypic characteristics of CA-MRSA lineages

ST	*arcC*	*aroE*	*glpF*	*gmk*	*pta*	*tpiA*	*yqiL*	*spa* type (Ridom)	*spa* type (eGenomics)	*spa* repeat pattern (eGenomics)	SCC*mec* type	Regional clones
1	1	1	1	1	1	1	1	t128	131	UJJFKBPE	IV	USA400, CMRSA7, WA-1
5	1	4	1	4	12	1	10	t002	2	TJMBMDMGMK	I, II, IV, V, VI	Geraldine, Pediatric
6	12	4	1	4	12	1	3	t207	*unk*	YHGFMBQBLOO	IV	
8	3	3	1	1	4	4	3	t008	1	YHGFMBQBLO	IV, V, VI	USA300, CMRSA10, WA-12
22	7	6	1	5	8	8	6	t005	113	TJEJNCMOMOKR	IV, V	
30	2	2	2	2	6	3	2	t019	19	XKAKAOMQ	IV, V	SWP, OSPC, WSPP, USA1100
45	10	14	8	6	10	3	2	t015	78	XKAKBEMBKB	IV, V, VI	
59	19	23	15	2	19	20	15	t216	17	ZDMDMNKB	IV, V	USA1000, Taiwan
72	1	4	1	8	4	4	3	t148	193	UJGFGMDMGGM	IV, V	USA700
75	36	3	43	34	39	52	49	*unk*	*unk*	Q2NMMMLMMJML	IV, V	WA-8, WA-79
78	22	1	14	23	12	53	31	t2815	*unk*	UEBBPB	IV	
80	1	3	1	14	11	51	10	t044	70	UJGBBPB	IV	European CA-MRSA
88	22	1	14	23	12	4	31	t186	9	UGFMEEBBPB	IV, V, VI	
91	1	26	28	18	18	54	50	t375	416	Y2EJCMBPB	II, IV, V	
93	6	64	44	2	43	55	51	t202	1143	YMJMMKKO	IV, V	Queensland
97	3	1	1	1	1	5	3	t267	105	UJGFMBBBPB	IV, V	
121	6	5	6	2	7	14	5	t159	312	I2Z2EGMMJH2M	V	
152	46	75	49	44	13	68	60	t355	207	UJ2GMKKPNSG	V	Balkan
377	46	75	49	50	13	68	60	t355	207	UJ2GMKKPNSG	V	Balkan
398	3	35	19	2	20	26	39	t011	*unk*	XKAOBQO	IV, V	LA-MRSA, ST398
772	1	1	1	1	22	1	1	t345	692	TJEFMBBPB	V	Bengal Bay, WA-60

Molecular characteristics of CA-MRSA strains listed in Table 2 and Figure 1. From left-to-right: (a) multilocus sequence typing (MLST) data, including sequence type and allele numbers for the 7 MLST housekeeping genes (*arcC-aroE-glpF-gmk-pta-tpiA-yqiL*); (b) representative *spa* type (Ridom and eGenomics) and *spa* repeat pattern (eGenomics), with 24-bp VNTR *spa* repeats denoted by letters; (c) SCC*mec* types known to be associated with each clonal lineage; (d) known regional clone names associated with a particular CA-MRSA lineage. ST, sequence type; *spa*, staphylococcal protein A; SCC*mec*, staphylococcal cassette chromosome *mec*; CMRSA, Canadian epidemic MRSA; WA, Western Australia; SWP, South West Pacific; OSPC, Oceanic Southwest Pacific; WSPP, Western Samoan Phage Pattern; LA-MRSA, livestock-associated MRSA; *unk*, unknown *spa* types or repeat patterns.

Mediavilla JR, et al.Current Opinion in Microbiology 2012, 15:588–595

First international spread and dissemination of the virulent Queensland community-associated methicillin-resistant *Staphylococcus aureus* strain

M. J. Ellington[1], M. Ganner[1], M. Warner[2], E. Boakes[1], B. D. Cookson[1], R. L. Hill[2] and A. M. Kearns[1]

Clin Microbiol Infect 2010; 16: 1009–1012

CA-MRSA lineages reported in the literature as of May 2012

ST	SCC*mec*	Country
ST1	IV	Abu Dhabi, Australia, Brazil, Canada, China, Denmark, Egypt, Finland, France, Germany, Greece, Ireland, Italy, Japan, Pakistan, Romania, Samoa, Singapore, South Korea, Switzerland, United Kingdom, United States
ST5	I	France, Iceland, South Africa
	II	Iceland, Japan
	IV	Algeria, Argentina, Australia, Austria, Azores, Canary Islands, China, France, Germany, Iceland, Italy, Morocco, Samoa, Senegal, Spain, Switzerland, United Kingdom
	V	Australia, Cameroon, Egypt, Japan, Nigeria
	VI	Azores, Spain
ST6	IV	Japan, Malaysia
ST8	IV	Abu Dhabi, Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Cameroon, Canada, Canary Islands, China, Colombia, Costa Rica, Cuba, Czech Republic, Denmark, Ecuador, Finland, France, French Polynesia, Gabon, Germany, Greece, Hong Kong, Iceland, India, Iraq, Ireland, Israel, Italy, Japan, Madagascar, Mexico, Netherlands, New Zealand, Nigeria, Norway, Pakistan, Peru, Poland, Portugal, Romania, Russia, Samoa, South Korea, Spain, Sweden, Switzerland, Trinidad & Tobago, United Kingdom, United States, Uruguay, Venezuela
	V	Germany, Nigeria
	VI	Portugal
ST22	IV	Australia, Azores, Canary Islands, Germany, India, Ireland, Japan, Netherland, Singapore, United Kingdom
	V	Germany
ST30	IV	Abu Dhabi, Australia, Austria, Brazil, Canary Islands, China, Czech Republic, Denmark, Egypt, Finland, France, French Polynesia, Germany, Hong Kong, Ireland, Italy, Japan, Kuwait, Latvia, Malaysia, Netherlands, New Zealand, Pakistan, Peru, Philippines, Poland, Romania, Russia, Samoa, Singapore, South Korea, Spain, Sweden, Switzerland, Taiwan, Turkey, United Kingdom, United States, Uruguay
	V	China, Madagascar
ST45	IV	Australia, Azores, Belgium, Germany, Hong Kong
	V	Australia, China, Hong Kong
	VI	Switzerland
ST59	IV	Australia, China, Denmark, Finland, Germany, Hong Kong, Netherlands, Singapore, Sweden, Taiwan, United Kingdom, United States, Vietnam
	V	Australia, China, Germany, Hong Kong, Japan, Poland, Singapore, Sweden, Taiwan, United Kingdom, United States, Vietnam
ST72	IV	Abu Dhabi, Czech Republic, Germany, Portugal, South Korea, Sweden, United States
	V	United States
ST75	IV	Australia
ST78	IV	Australia
ST80	IV	Abu Dhabi, Algeria, Australia, Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Egypt, Finland, France, Germany, Greece, Ireland, Israel, Italy, Jordan, Kuwait, Lebanon, Libya, Malta, Netherlands, Norway, Poland, Portugal, Romania, Singapore, Slovenia, Spain, Sweden, Switzerland, Tunisia, United Kingdom
ST88	IV	Abu Dhabi, Angola, Cameroon, China, Gabon, Italy, Japan, Madagascar, Mali, Netherlands, Niger, Nigeria, Portugal, Senegal, Spain, Sweden, United Kingdom
	V	China, Italy, Madagascar, Sweden
ST91	II	Japan
	IV	Japan
	V	Japan
ST93	IV	Australia, Czech Republic, Finland, Italy, Netherlands, Samoa, United Kingdom
ST97	IV	Abu Dhabi, Canary Islands, Denmark, Germany, Netherlands
	V	Egypt, Kuwait, United Kingdom
ST121	V	Australia, Cambodia
ST152	V	Austria, Canary Islands, Denmark, Germany, Kosovo, Macedonia, Slovenia, Sweden, Switzerland
ST377	V	Australia, France, Greece, Netherlands, Switzerland
ST398	II	Hong Kong
	IV	Austria, Belgium, China, Denmark, Germany, Hong Kong, Italy, Netherlands
	V	Austria, Belgium, Canada, China, Denmark, Germany, Hong Kong, Italy, Netherlands, Norway, Portugal, Spain, Sweden, United States
	NT	Belgium, Denmark, Germany, Netherlands
ST772	IV	India
	V	Abu Dhabi, Australia, Bangladesh, Finland, Germany, Hong Kong, India, Ireland, Italy, Japan, Netherlands, United Kingdom

In Turkey

- ✓ Antalya
  - 2 / 30 CA-MRSA
  - SCCtypeIV , PVL (+)

Baran C, et al. Mikrobiyol Bul 2010; 44: 533-545

- ✓ *S. aureus*, Ankara
  - 285 SSTI; 161 control
  - 4 SCCtypeIV
  - 10 PVL (+); all MSSA

Gülmez D, et al. Mikrobiyol Bul 2012; 46(3): 341-351

J Antimicrob Chemother 2012; **67**: 837–840
doi:10.1093/jac/dkr568 Advance Access publication 11 January 2012

Journal of Antimicrobial Chemotherapy

Panton–Valentine leucocidin gene carriage among *Staphylococcus aureus* strains recovered from skin and soft tissue infections in Turkey

Tulin Demir[1]*, Nilay Coplu[2], Hasan Bayrak[3], Meral Turan[1], Tuncay Buyukguclu[4], Neriman Aksu[5], Meral Eksioglu[6], Basak Yalcin[7], Nilgün Atakan[8], Selcuk Kilic[2], Zeynep Ceren Karahan[9] and Berrin Esen[2]

- ✓92 CA and 150 HA – S.aureus
  - 77 / 242 were mecA positive.
    - All PVL (-)
  - 22 / 165 MSSA were PVL (+)
    - 5.3% HA-MSSA
    - 15.2% CA-MSSA

USA300

CA-MRSA strain which appears to pose a global epidemic threat

- ✓ College football team in Pennsylvania
- ✓ Outbreaks among prisoners Mississippi and Los Angeles
- ✓ Risk groups
  - military personnel,
  - prisoners,
  - athletes,
  - intravenous drug users,
  - the homeless, urban populations,
  - and men who have sex with men
- ✓ Primary cause od SSTI in general population

Tenover FC, Goering RV.JAC 2009, 64:441-446.
Nimmo GR. Clin Microbiol Infect 2012, 18:725-734.

Travel of USA300

arginine catabolic mobile element (ACME)

→ heightened transmissibility

- ✓ Among high-risk groups in Vancouver,
  - the primary strain in Canada (CMRSA-10)
- ✓ Increasingly reported in
  - Europe,
  - Japan
  - Australia
- ✓ USA300-like strains (SCCmec IVc)
  - Colombia & neighboring countries
  - Both community and hospital acquired

Tenover FC, Goering RV.JAC 2009, 64:441-446.
Nimmo GR. Clin Microbiol Infect 2012, 18:725-734.
Nichol KA, Diagn Microbiol Infect Dis 2011, 69:320-325.
Reyes J, et al. CID 2009,49:1861-1867.

JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 2011, p. 433–436
0095-1137/11/$12.00 doi:10.1128/JCM.02201-10

Vol. 49, No. 1

Molecular Epidemiology of Panton-Valentine Leukocidin-Positive *Staphylococcus aureus* in Spain: Emergence of the USA300 Clone in an Autochthonous Population▽

Raquel Blanco,[1]† Anne Tristan,[2,3] Guillermo Ezpeleta,[1] Anders Rhod Larsen,[4] Michèle Bes,[2,3] Jérôme Etienne,[2,3] Ramon Cisterna,[1] and Frédéric Laurent[2,3]*

Occurrence of the USA300 community-acquired *Staphylococcus aureus* clone in Austria

TABLE

Summary data on nine isolates of CA-MRSA USA300 in Austria. All isolates showed SCC*mec* type IVa and were of *spa* type t008

Isolate ID	Year of isolation	Clinical presentation	Age/Gender	Epidemiological links to America	ACME gene cluster	Antibiotic Resistance
A	2004	abscess right thigh	51/M	-	+	ERY, CIP1
B	2004	abscess bartholinic gland	33/F	-	+	ERY, CIP, MFL
C	2004	asymptomatic carrier; husband of patient B	38/M	-	+	ERY, CIP, MFL
D	2005	abscess axilla	52/F	professional contact with mail from US	-	ERY, CIP1
E	2005	abscess perineal	58/M	-	-	ERY, CIP1
F	2005	infected vascular ulcer, lower leg	76/M	-	+	ERY, CIP, MFL
G	2005	abscess axilla	20/F	exchange student, US citizen	+	ERY, CIP, MFL, TET
H	2005	multiple abscesses, gluteal region and lower leg	76/M	-	+	ERY, CIP, MFL
I	2006	abscess after insect bite	26/M	status post vacation in Central America	+	ERY, CIP1

Eurosurveillance 12 (43), 2007

Importance of USA300

- ✓ Preferentially colonize extranasal sites
- ✓ Environmental transmission via fomites has been implicated
- ✓ Cause of serious invasive disease
  - CAP
  - Endocarditis
  - Necrotizing fasciitis
- ✓ Progressively becoming endemic in nosocomial settings,
  - displacing ST5-II as the primary cause of bloodstream infection in parts of the U.S.
- ✓ Acquiring greater antibiotic resistance
  ‘multidrug-resistant’

JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 2009, p. 73–78
0095-1137/09/$08.00+0 doi:10.1128/JCM.01557-08

Vol. 47, No

Emergence and Characterization of Community-Associated Methicillin-Resistant *Staphyloccocus aureus* Infections in Denmark, 1999 to 2006[▽]

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National Center for Antimicrobials and Infection Control, Statens Serum Institut, Copenhagen, Denmark

Received 12 August 2008/Returned for modification 7 October 2008/Accepted 17 October 2008

The epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA) infections has changed worldwide. From being strictly nosocomial, MRSA is now frequently found as a community-associated (CA) pathogen. Denmark has been a low-prevalence country for MRSA since the mid-1970s but has in recent years experienced an increasing number of CA-MRSA cases. The aim of this study was to describe the emergence of CA-MRSA infections in Denmark. All Danish MRSA specimens and corresponding clinical data from 1999 to 2006 were investigated. Isolates were analyzed by antibiotic resistance and molecular typing and were assigned to clonal complexes (CC). Clinical data were extracted from discharge summaries and general practitioners' notes, from which assessments of community association were made for all infected cases. CA-MRSA cases constituted 29.4% of all MRSA infections (n = 1,790) and an increasing proportion of the annual numbers of MRSA infections during the study period. CA-MRSA was associated with a young age, skin and soft tissue infections, and non-Danish origin. Transmission between household members was frequently reported. Molecular typing showed >60 circulating clones, where 89.4% of the isolates belonged to five CC (CC80, CC8, CC30, CC5, and CC22), 81.2% carried staphylococcal cassette chromosome *mec* IV, and 163/244 (69.4%) were positive for Panton-Valentine leukocidin. Clinical and microbiological characteristics indicated that import of MRSA occurs frequently. Resistance to ≥3 antibiotic classes was observed for 48.8% of the isolates. The emergence of CA-MRSA in Denmark was caused by diverse strains, both well-known and new CA-MRSA strains. The results suggest multiple introductions of MRSA as an important source for CA-MRSA infections in Denmark.

JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 2007, p. 2554–2563 Vol. 45, No. 8
0095-1137/07/$08.00+0 doi:10.1128/JCM.00243-07

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

Angela S. Rossney,[1,2] Anna C. Shore,[3] Pamela M. Morgan,[1] Margaret M. Fitzgibbon,[1,2] Brian O'Connell,[1,2] and David C. Coleman[3]*

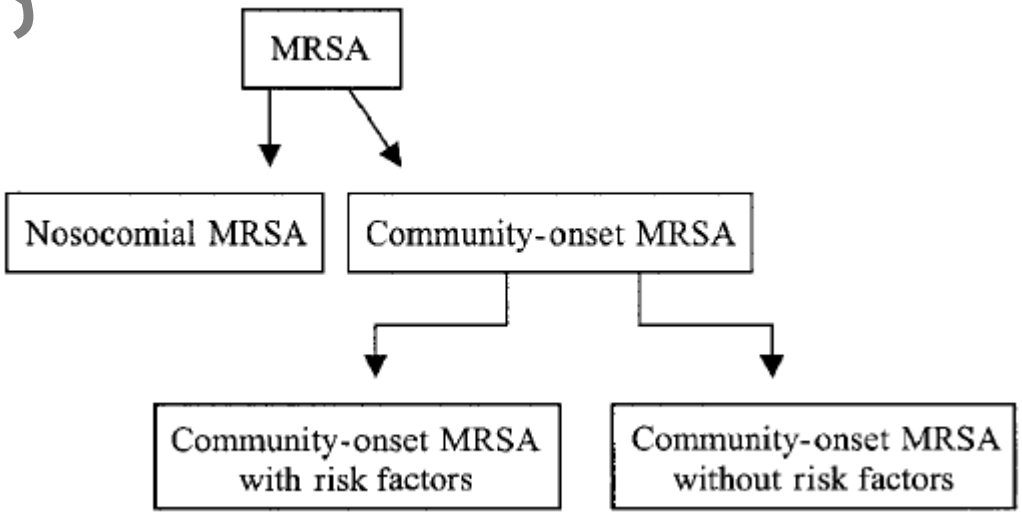
- ✓ 25 / 1389 MRSA are PVL (+)
  - ST30, ST8, ST 22,ST80, ST5, ST14
  - 19 / 25 (%79) CA-MRSA
  - 13 / 25 (%52) non Irish ethnic groups
- ✓ 30 CA-MRSA
  - 2 / 30 (%6.7) PVL (+)

Community-Acquired Methicillin-Resistant *Staphylococcus aureus*: A Meta-Analysis of Prevalence and Risk Factors

Cassandra D. Salgado, Barry M. Farr, and David P. Calfee
University of Virginia Health System, Charlottesville

Clinical Infectious Diseases 2003; 36:131–9

- ✓ **30%-37% of all hospitalized MRSA patients are CA**



JCM

Emergence of Hospital- and Community-Associated Panton-Valentine Leukocidin-Positive Methicillin-Resistant *Staphylococcus aureus* Genotype ST772-MRSA-V in Ireland and Detailed Investigation of an ST772-MRSA-V Cluster in a Neonatal Intensive Care Unit

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- ✓ Resistant to
  - Makrolides
  - Aminoglycosides
- ✓ **PVL (+), enterotoxin gene (+), immun evasion complex genes (+)**
- ✓ **May have been imported from India in several occasions**

Journal of Clinical Microbiology p. 841–847 **,2011**

Risk factors for CA-MRSA

- ✓ History of MRSA infection or colonization in patient or close contact
- ✓ High prevalence of CA MRSA in local community or patient population
- ✓ Recurrent skin disease
- ✓ Crowded living conditions (e.g. homeless shelters, military barracks)
- ✓ History of incarceration
- ✓ Participation in contact sports
- ✓ Skin or soft tissue infection with poor response to B-lactam antibiotics
- ✓ Recent and/or frequent antibiotic use
- ✓ Injection drug use
- ✓ Child under age 2 years
- ✓ Male with history of having sex with men
- ✓ Shaving of body hair

Wisconsin Division of Public Health

Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections in Adults and Children

Catherine Liu,[1] Arnold Bayer,[3,5] Sara E. Cosgrove,[6] Robert S. Daum,[7] Scott K. Fridkin,[8] Rachel J. Gorwitz,[9] Sheldon L. Kaplan,[10] Adolf W. Karchmer,[11] Donald P. Levine,[12] Barbara E. Murray,[14] Michael J. Rybak,[12,13] David A. Talan,[4,5] and Henry F. Chambers[1,2]

- ✓ For empriric coverage of CA-MRSA (OP-oral)
  - Clindamycin (A-II),
  - TMP-SMX (A-II),
  - Doxycycline / minocycline (A-II),
  - Linezolid (A-II).

Clinical Infectious Diseases 2011;52(3):e18–e55

For hospitalized patients with complicated SSTI

- ✓IV vancomycin (A-I),
- ✓PO / IV linezolid (A-I),
- ✓IV daptomycin (A-I)
- ✓IV telavancin (A-I),
- ✓PO / IV clindamycin (A-III).
- ✓A b-lactam antibiotic (eg, cefazolin)

Liu,et al. Clinical Infectious Diseases 2011;52(3):e18–e55,

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Complementary Therapies in Clinical Practice
Volume 14, Issue 2 , Pages 77-82, May 2008

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Antibacterial activity of honey against community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA)

Yasunori Maeda, Anne Loughrey, J.A. Philip Earle, B. Cherie Millar, Juluri R. Rao, Angela Kearns, Ogie McConville, Colin E. Goldsmith, Paul J. Rooney, James S.G Dooley, Colm J. Lowery, William J. Snelling, Ann McMahon, David McDowell, John E. Moore

Abstract | Full Text | PDF | References

Summary

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has now been described globally, as a clinically significant pathogen, particularly associated with skin and soft tissue infections, including abscesses, cellulitis and furunculosis. The recent emergence of CA-MRSA combined with its predominant presentation associated with skin and soft tissue infection, the previous literature indicating honey as an effective treatment of healthcare-associated HA-MRSA-related wound infection, as well as honey's ease of topical application, make the current study timely and of interest to healthcare practitioners involved with wound management. Although previous studies have examined the antimicrobial activity of honey

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Take Home message

- ✓ The rapid dissemination of CA-MRSA since the early 2000s and the appearance of new successful lineages is a matter of concern.
- ✓ Dissemination of USA300, acquiring greater antibiotic resistance is a matter of another concern.
- ✓ HCA-Serious infections with resistant isolates would be much more prevalant in the future
- ✓ Given the rapid spread and the high virulence of CA-MRSA, global strategies are needed.