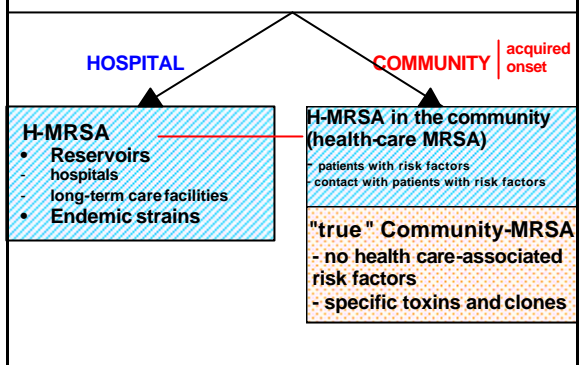


Infections communautaires à *Staphylococcus aureus* résistant à la métilcilline

INSERM E0230, Lyon, France

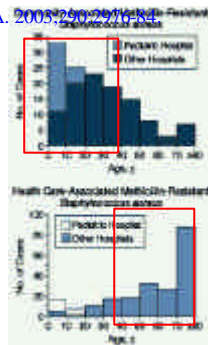
Epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA)



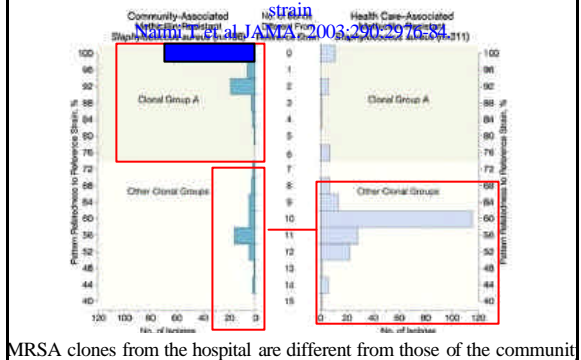
Median age of patients with C- and H-MRSA

Naimi T et al JAMA. 2003;290:2976-84

- Community-associated MRSA patients are younger than health care-associated MRSA patients (median age, 23 years vs 68 years, $P < .001$)



PFGE pattern relatedness of C- and H-MRSA to a reference strain



Panton Valentine leukocidin genes are more frequently detected in C-MRSA than in H-MRSA

Naimi T et al JAMA. 2003;290:2976-84

Table 4. Community-Associated and Health Care-Associated Methicillin-Resistant *Staphylococcus aureus* Cases, by Infection Type

Gene Sequence	No. (%) of Cases With Gene Sequence		Odds Ratio (95% Confidence Interval)*
	Community-Associated (n = 78)	Health Care-Associated (n = 26)	
Ecotoxin Genes†			
<i>β-haemolysin</i>	2 (3)	0	Localized
<i>γ-haemolysin</i>	55 (96)	26 (100)	2.40 (1.03)
<i>β-lactoglobulin</i>	32 (92)	26 (100)	2.40 (1.03)
<i>PVL</i>	50 (71)	1 (4)	5.01 (1.40-5.25)
<i>exf1</i>	10 (68)	1 (4)	3.03 (1.22-3.95)
<i>exf2</i>	8 (23)	1 (4)	5.35 (1.30-5.14)
<i>exf3</i>	13 (50)	0	Localized
<i>exf4</i>	5 (19)	14 (54)	0.41 (0.12-0.90)
<i>exf5</i>	5 (19)	25 (96)	0.17 (0-0.57)
<i>exf6</i>	17 (55)	1 (4)	5.53 (1.47-3.94)
<i>exf7</i>	5 (19)	25 (96)	0.17 (0-0.57)
<i>exf8</i>	5 (19)	14 (54)	0.41 (0.13-0.98)
<i>exf9</i>	10 (62)	0	Localized
<i>exf10</i>	5 (19)	26 (96)	0.17 (0-0.57)
<i>exf11</i>	5 (19)	25 (96)	0.17 (0-0.57)
<i>exf12</i>	5 (19)	26 (96)	0.17 (0-0.57)
Gene Alleles‡			
<i>SCC1A</i>	22 (28)	25 (96)	0.22 (0-0.77)
<i>SCC2</i>	17 (85)	1 (5)	3.03 (1.47-3.85)
<i>SCC3</i>	3 (15)	24 (95)	0.16 (0-0.56)
<i>SCC4</i>	22 (85)	3 (12)	5.07 (1.47-3.95)

Type of infections in patients with C or H-MRSA

Table 4. Community-Associated and Health Care-Associated Methicillin-Resistant *Staphylococcus aureus* Cases, by Infection Type

Infection Type*	No. (%) of Methicillin-Resistant <i>S aureus</i> Cases		P Value†
	Community-Associated (n = 131)	Health Care-Associated (n = 837)	
Skin/soft tissue	98 (75)	343 (37)	<.001
Otitis media/externa	17 (13)	11 (1)	<.001
Respiratory tract‡	8 (6)	205 (22)	<.001
Bloodstream	5 (4)	83 (9)	.07
Urinary tract‡	1 (1)	185 (20)	<.001
Other§	10 (8)	110 (12)	.21

*If patients had more than 1 type of infection, only 1 was selected for inclusion in this table. The hierarchy for choosing the type of infection for patients with multiple sources was: bacteremia, bone, pleural fluid, peritoneal fluid, joint, surgical specimen, postoperative wound, eye, ear, apical, urine, and skin.

†Refers to the statistical probability that the type of infection among community-associated cases differed from the percentage among health care-associated cases ($\alpha = .05$).

‡Among health care-associated isolates, some respiratory tract isolates were obtained from endotracheal tubes, and some urinary tract isolates were obtained from Foley catheters.

§Included bone, peritoneal fluid, joint, surgical specimen, and postoperative wound.

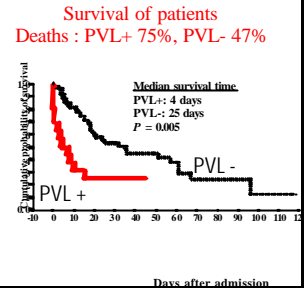
Community-acquired infections due to Pantone-Valentine leukocidin+ MRSA (primary skin infections)

Couppié *et al.* 1994
Arch. Dermatol.; Lina *et al.* 1999 Clin. Infect. Dis.



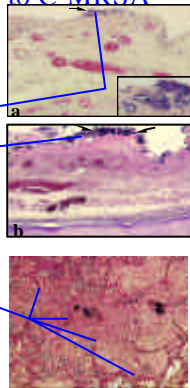
Necrotizing pneumonia caused by *S. aureus* strains carrying PVL-genes (Gillet *et al.* 2002 Lancet)

- Healthy children and young adults
- Preceded by influenza-like symptoms
- Rapidly progressive, haemorrhagic
- initial leukopenia
- Lethality rate 75 %

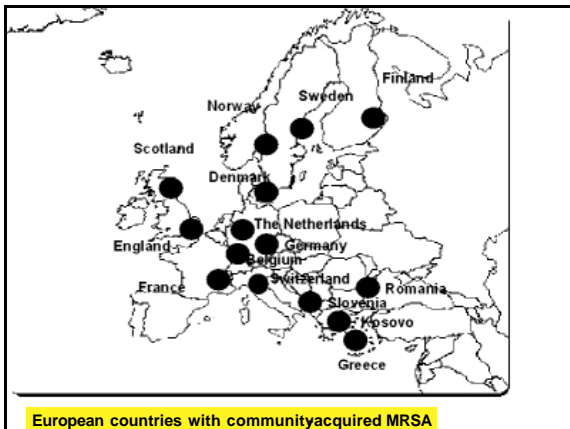


Necrotizing pneumonia due to C-MRSA

- 1. Adhesion of Gram+ cocci on respiratory epithelium
 - Larynx
 - Trachea
- 2. Necrotizing lesions of the lungs with destruction of the alveolar septa



The intercontinental emergence of community-MRSA (distinct of hospital-MRSA)



PVL+ C-MRSA are transmitted Los Angeles Times

•It appears to be spread primarily **by skin-to-skin contact**, including sex.

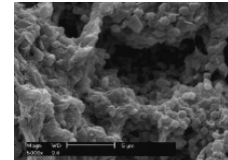


•Spread may also occur **through indirect contact by touching objects** (i.e., towels, sheets, wound dressings, clothes, workout areas, sports equipment) contaminated by the infected skin of a person with MRSA.

Transmission of C-MRSA after skin-to-skin contact during a match

Transmission of C-MRSA through indirect contact by touching objects

- Scanning electron microscopy of wood sample taken from the seating area of a sauna with known MRSA-positive surface culture (from Baggett HC et al J Infect Dis. 2004;189:1565-73)



Outbreaks with C-MRSA

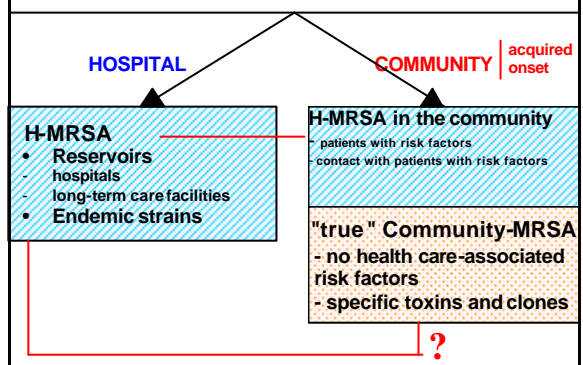
Los Angeles Times

Outbreaks, sometimes with fatalities, have been reported among intravenous drug abusers, athletes, prisoners, Native Americans and Eskimos, whose close living conditions make them likely to share personal items such as towels.



Outbreaks in Los Angeles County jail during 2002, in gay communities.

Epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA)



Association of the European PVL+ MRSA clone with hospital-acquired infections

- in Greece (de Sousa M et al JCM 2003;42:27-32)
 - premature baby one week after birth (1998)
 - 10 isolates in 2000, 3-20 days after admission to hospital
- in Algeria (N. Ramdani)
 - 10 of 12 isolates were hospital-acquired

Hospital transmission of PVL+ MRSA among post-partum women

- Saiman L et al: CID 2003;15:1313-9
 - 8 postpartum women (NY, USA), route of transmission not discovered
- France, city of Lannion, 47 cases in 12 familial clusters with a cross-contamination in the maternity of Lannion.

Molecular epidemiology of community-acquired MRSA isolates and its evolution

Genes ^a	CO-MRSA isolates from					Total n=117 (%)
	France-Switzerland n=67 (%)	USA n=29 (%)	USA n=4 (%)	Oceania ^b Southwest Pacific clone n=13 (%)	Australia Queensland clone n=4 (%)	
Sequence type	80	1	59 or 8	30	93	
Pulsotypes	A1-A7	B1-B5	D1- D2	C1- C3	E1	
agr group	3	3	1	3	3	
SCCmec type IV	67 (100)	29 (100)	4 (100)	13 (100)	4 (100)	117 (100)
Leukocidins PVL genes	67 (100)	29 (100)	4 (100)	13 (100)	4 (100)	117 (100)
Enterotoxins						
ssa	0 (0)	23 (79)	0 (0)	0 (0)	0 (0)	23 (20)
seb	0 (0)	8 (28)	1 (25)	0 (0)	0 (0)	9 (8)
sec	0 (0)	20 (69)	0 (0)	0 (0)	0 (0)	20 (17)
sed-sej	0 (0)	0 (0)	3 (75)	0 (0)	0 (0)	3 (3)
seh	0 (0)	29 (100)	0 (0)	0 (0)	0 (0)	29 (25)
sek	0 (0)	24 (83)	0 (0)	0 (0)	0 (0)	24 (21)
agr	0 (0)	0 (0)	0 (0)	13 (100)	0 (0)	13 (11)

Vandenesch et al. EID, 2003;9:978-84

ST	Country or continent of detection	agr group
	USA Europe Oceania Africa Asia	
ST1	USA ++	3
ST8	USA +++ The Netherlands France Switzerland	1
ST22	The Netherlands	1
ST30	USA +++ The Netherlands Australia, New Zealand, Tahiti, Samoa	3
ST37	The Netherlands	3
ST59	USA + The Netherlands	1
ST72	USA +	
ST80	Europe +++ Algeria	3
ST93	Australia	3
ST5	Switzerland Algeria	2
ST 677	The Netherlands, Switzerland, France	1

The different clones of PVL+ CA-MRSA (6 ST's in 2003, 11 ST's in 2004)

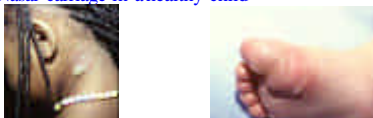
2003-2004

Beside PVL, other *S. aureus* toxins are associated with C-MRSA clones

Exfoliative positive C-MRSA

Liassine N et al JCM 2004;42:825-8

- First description by Yamaguchi et al in Japan (JID, 2002, 185:1511-6)
- Two isolates in Switzerland
 - exfoliatin A positive
 - same PFGE and ST88 type as isolates from Japan
- One similar isolate in Portugal
 - Nasal carriage in a healthy child

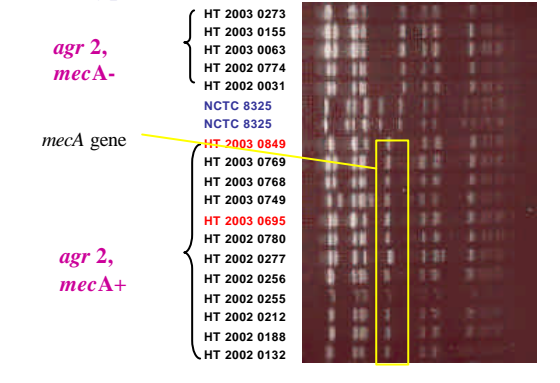


Toxic shock syndrome toxin positive MRSA (ST5)

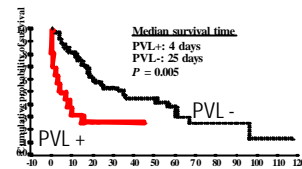
	agr1	agr2	agr3	Total
mecA-	1	5	69	75
mecA+	0	25	2	27
Total	1	30	71	102

agr alleles and mecA gene in tst+ *S. aureus* strains (France 2002-2003)

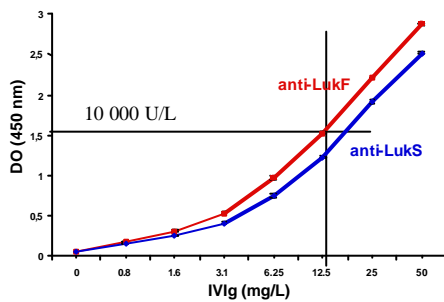
PFGE types of *tst+* *S. aureus* isolates



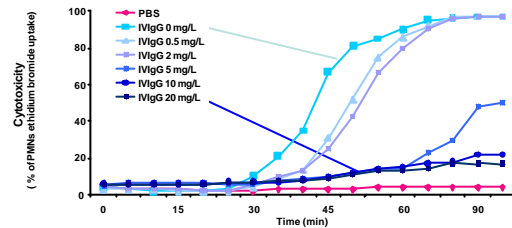
Could we use IVIg to block the effect of PVL ?



Commercial intravenous immunoglobulins (IVIg) contains PVL-specific antibodies JID, 2004,189:346-53



IVIg inhibition of PVL-induced ethidium bromide uptake by PMNs



In summary

- True C-MRSA are emerging from all over the world
 - Appear to be highly successful in spreading in the community
 - Are beginning to spread in hospitals (maternity)
 - Harbour continent-specific STs which are now spreading oversea and are diversifying
 - Contain SCC *mec* type IV
 - Contain the PVL genes or occasionally the exfoliatin toxin gene or the toxin shock syndrome toxin gene
 - PVL is a highly virulent leading to necrosis at high dose. Its action can be blocked by IVIg