New virulent strains of *S.aureus* in Belgium

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National MRSA Surveillance in Belgium

- 5 clinical non duplicate MRSA strains
- Participation : from 85 hospitals in 1995 to 106 hospitals in 2003
- 1741 MRSA strains (range from 384 to 512/year)
- Molecular typing
  - PFGE after *Sma*I macrorestriction
  - *SCCmec* typing
  - MLST

Deplano et al *Clin Microbiol Infect* 2000;6:239

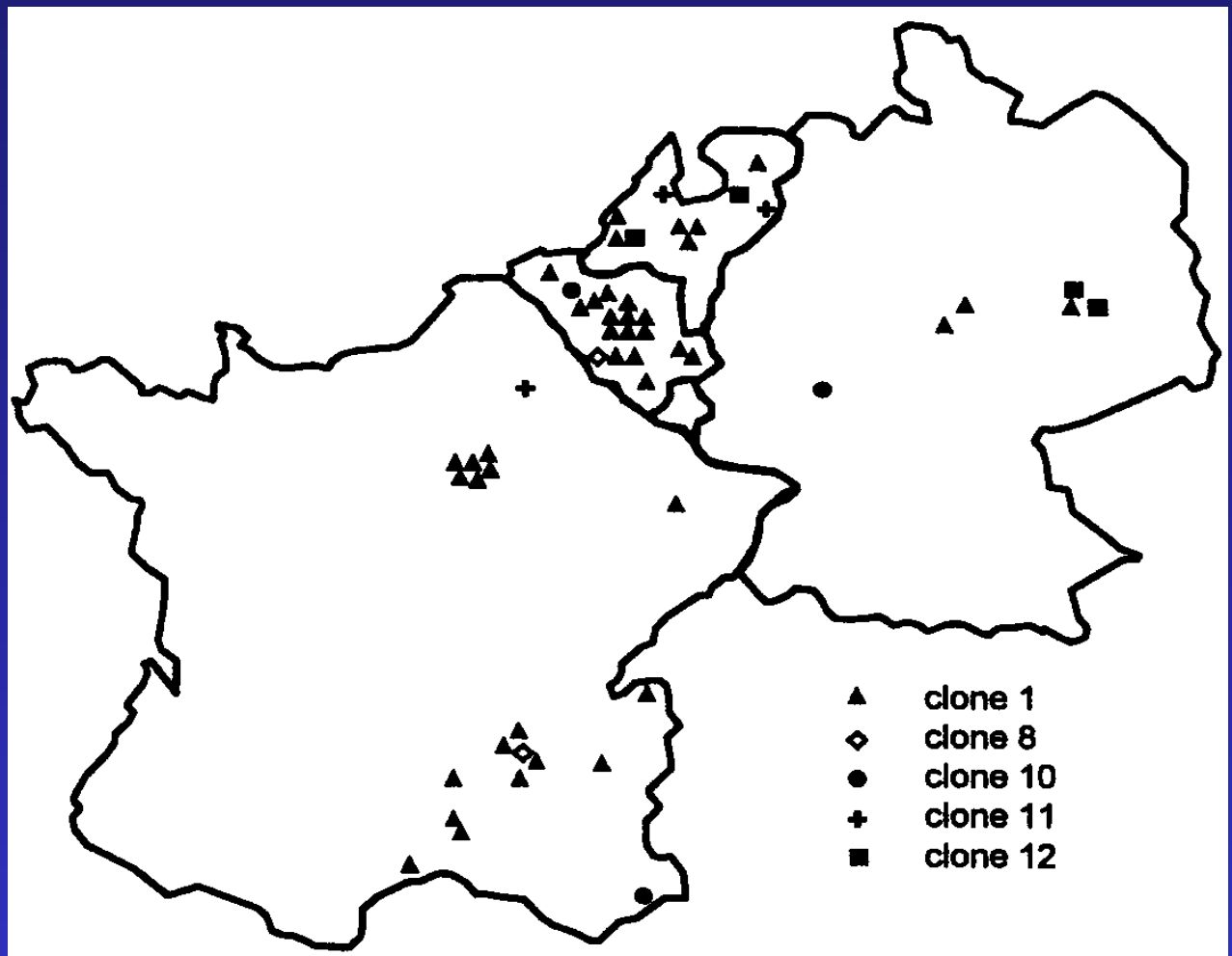
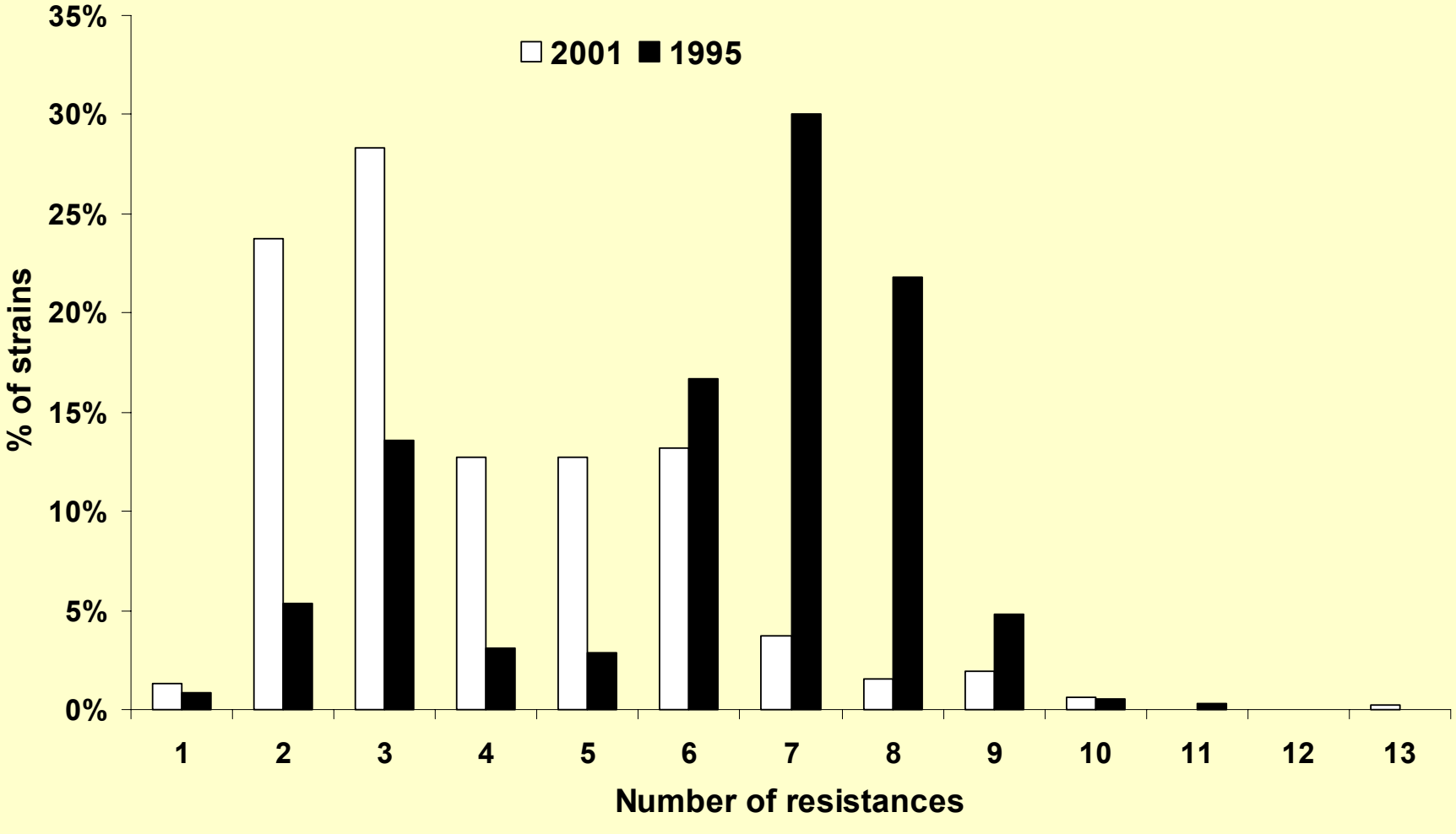
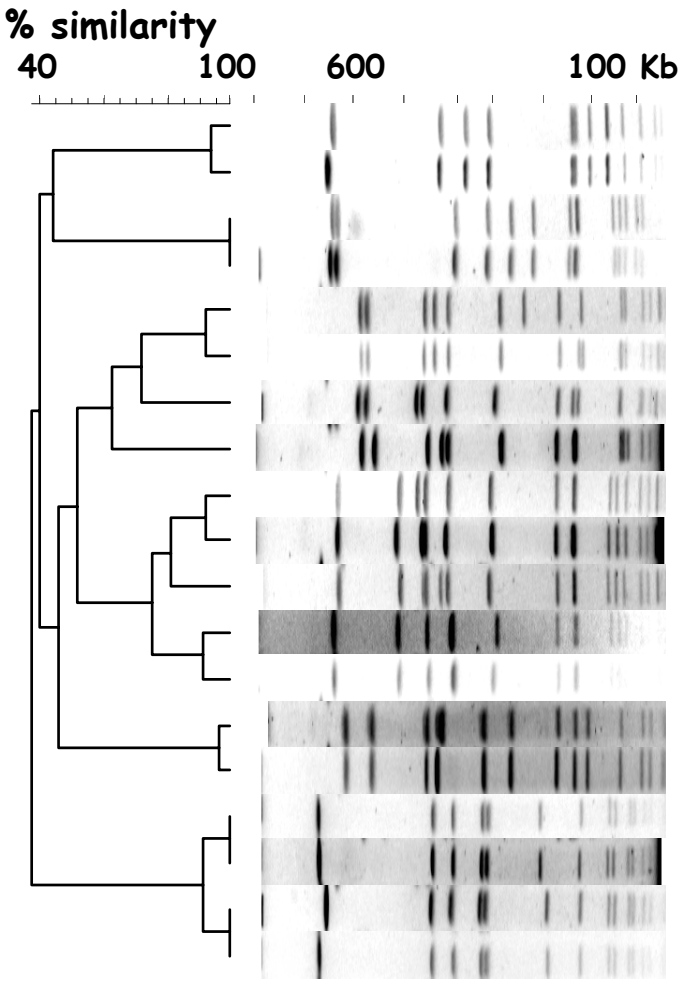


Figure 2 Map of Belgium, France, Germany and The Netherlands, indicating the area of dissemination of international epidemic MRSA clones.

MRSA strains resistant to antimicrobials, Belgium, National Surveys 1995 -2001



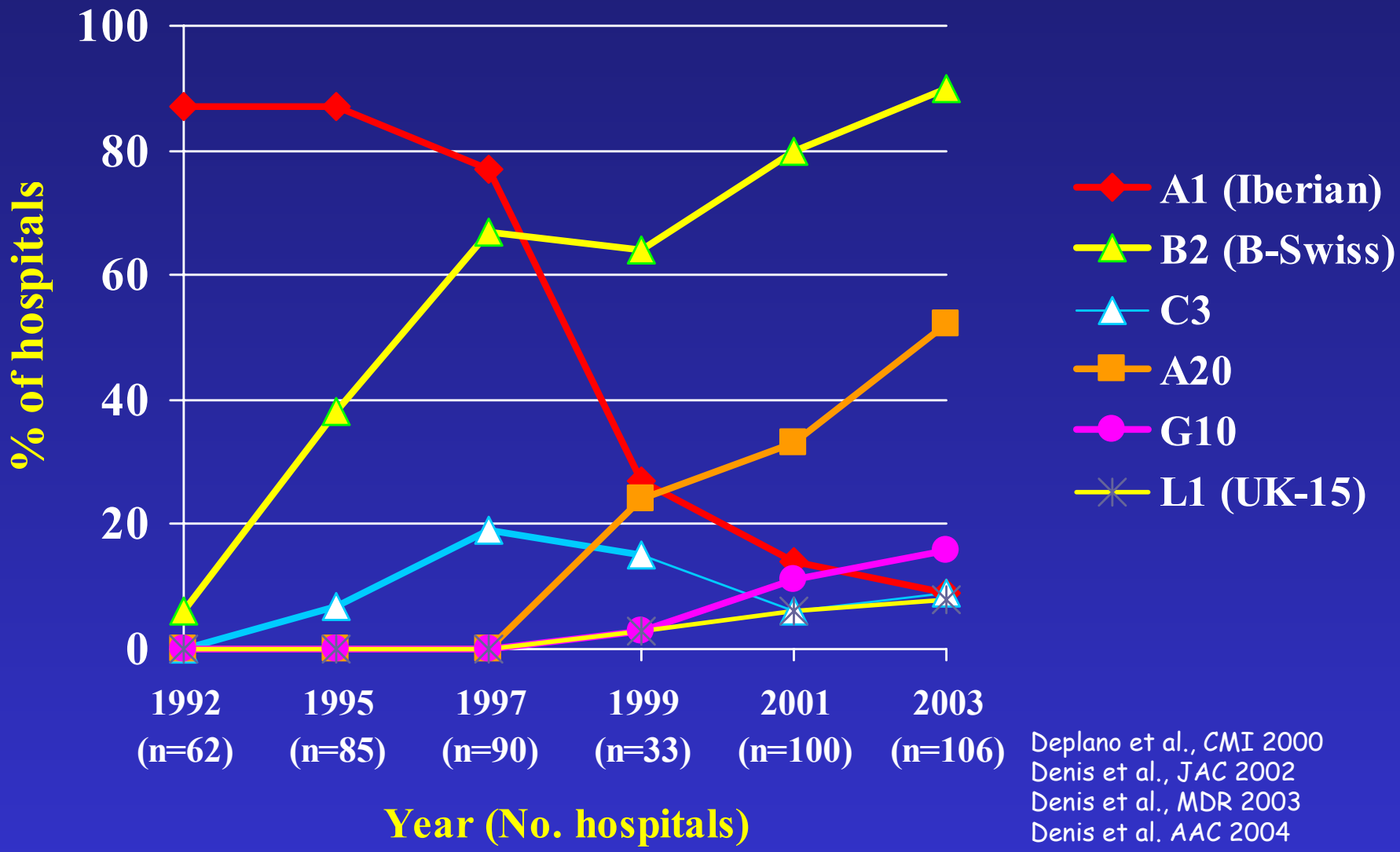
Correlation between PFGE types, MLST and SCCmec of 8 epidemic MRSA types in Belgium



PFGE Gr./type	MLST Profile	MLST Type	MLST CC	SCCmec Type
J1	2-2-2-2-2-3-2	36	30	II
J1	2-2-2-2-2-3-2	36	30	II
L1	7-6-1-5-8-8-6	22	22	IV
L1	7-6-1-5-8-8-6	22	22	IV
D7	1-4-1-4-12-24-29	228	5	I
D7	1-4-1-4-12-24-29	228	5	I
D4	1-4-1-4-12-24-29	228	5	I
C3	1-4-1-4-12-1-10	5	5	IV
A1	3-3-1-12-4-4-16	247	8	I
A1	3-3-1-12-4-4-16	247	8	I
A1	3-3-1-12-4-4-16	247	8	I
A20	3-3-1-1-4-4-3	8	8	IV
A20	3-3-1-1-4-4-3	8	8	IV
G10	1-4-1-4-12-1-10	5	5	II
G10	1-4-1-4-12-1-10	5	5	II
B2	10-14-8-6-10-3-2	45	45	IV
B2	10-14-8-6-10-3-2	45	45	IV
B2	10-14-8-6-10-3-2	45	45	IV
B2	10-14-8-6-10-3-2	45	45	IV

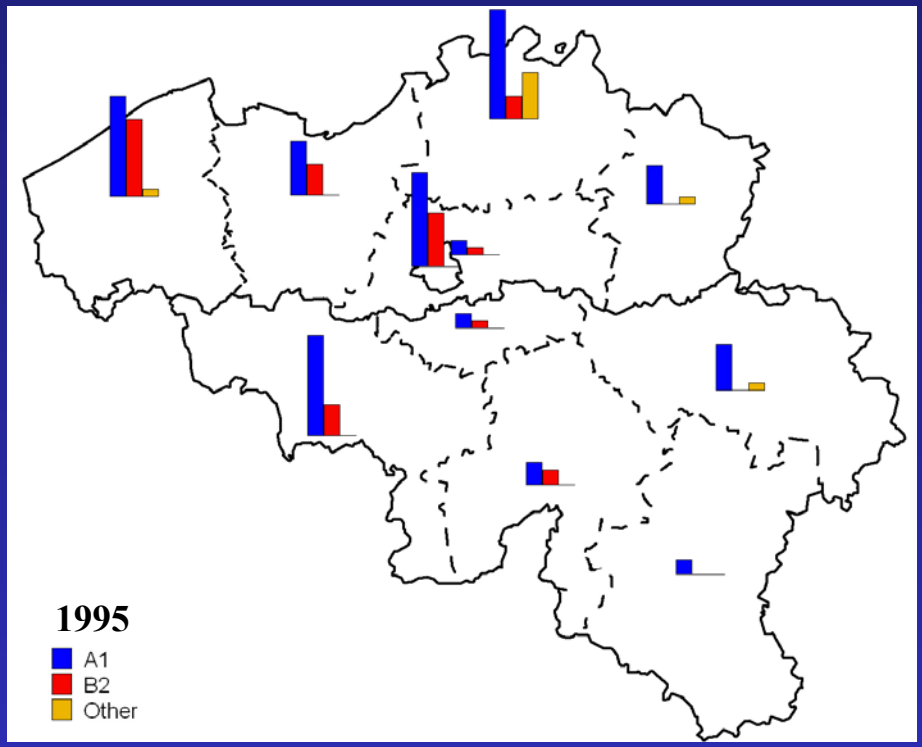
Distribution of Epidemic MRSA PFGE Types

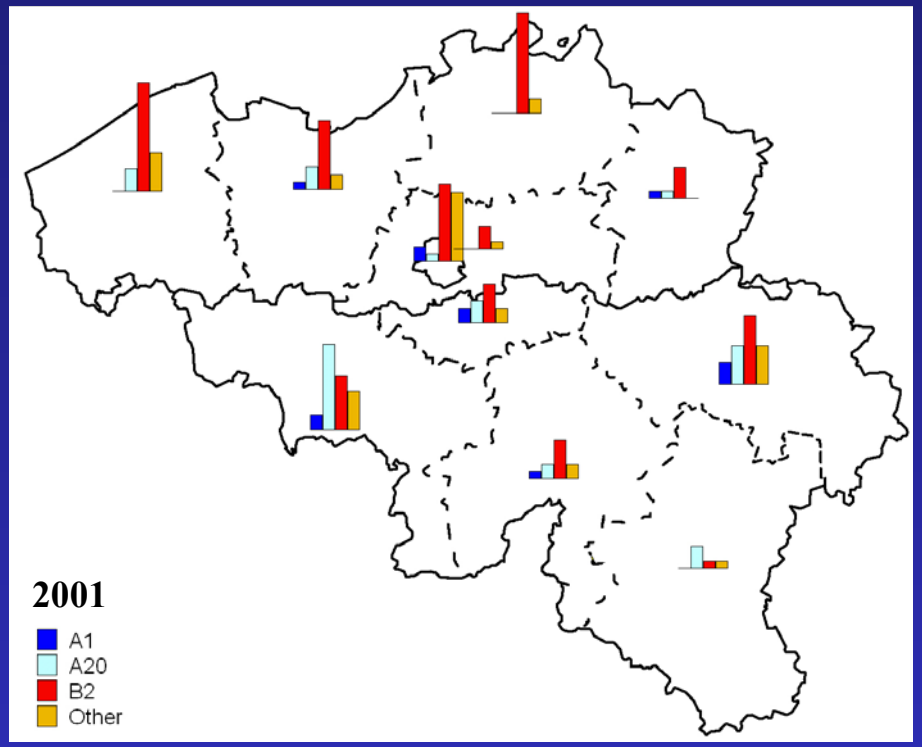
National Surveillance, Belgium, 1992-2003



Deplano et al., CMI 2000
Denis et al., JAC 2002
Denis et al., MDR 2003
Denis et al. AAC 2004

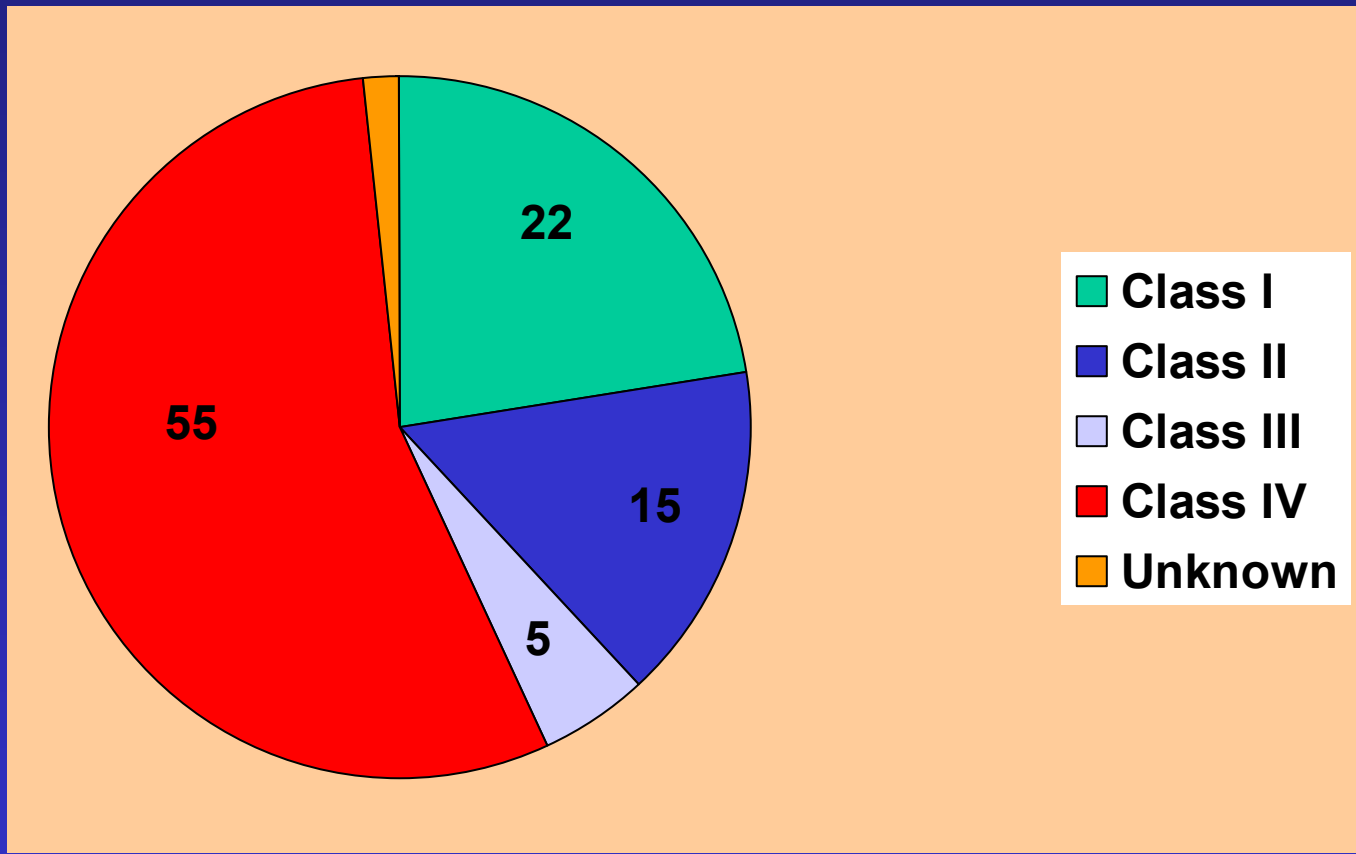
Evolution of geographic distribution by province of epidemic MRSA PFGE types A1, A20, B2 and other

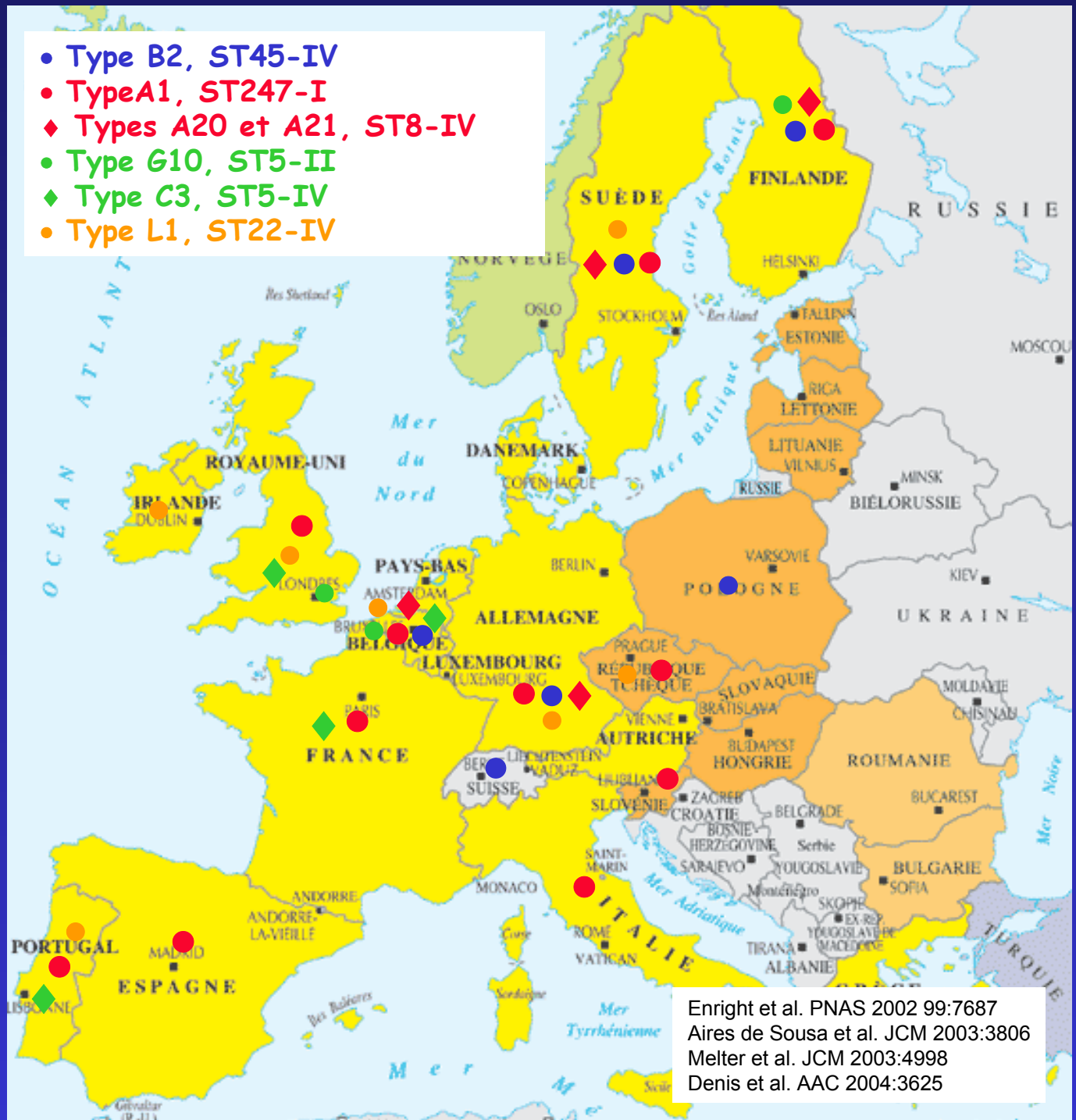




Denis O. et al. AAC 2004:3625

SCC*mec* distribution among nosocomial MRSA types Belgium, 2001





Enright et al. PNAS 2002 99:7687
Aires de Sousa et al. JCM 2003:3806
Melter et al. JCM 2003:4998
Denis et al. AAC 2004:3625

Mechanisms of disease

Association between *Staphylococcus aureus* strains carrying gene for Panton-Valentine leukocidin and highly lethal necrotising pneumonia in young immunocompetent patients

Yves Gillet, Bertrand Issartel, Philippe Vanhems, Jean-Christophe Fournet, Gerard Lina, Michèle Bes, François Vandenesch, Yves Piémont, Nicole Brousse, Daniel Floret, Jerome Etienne

Summary

Background Between 1986 and 1998, eight cases of

Introduction

Staphylococcus aureus is responsible for about 2% of cases of community-acquired pneumonia[1] and at least 10% of cases

Community-Acquired Methicillin-Resistant *Staphylococcus aureus* Carrying Panton-Valentine Leukocidin Genes: Worldwide Emergence

François Vandenesch,* Timothy Naimi,† Mark C. Enright,‡ Gerard Lina,* Graeme R. Nimmo,§ Helen Heffernan,¶ Nadia Liassine,# Michèle Bes,* Timothy Greenland,** Marie-Elisabeth Reverdy,* and Jerome Etienne*

Gillet Y et al. The Lancet 2002:359
Vandenesch F. et al. Emerging Infectious Diseases 2003: 9

Community-Acquired PVL + MRSA : Furonculosis & Necrotizing Pneumonia

Emergence since 1990s
Australia, USA, Asia, Europe
Healthy children & young adults
New disease

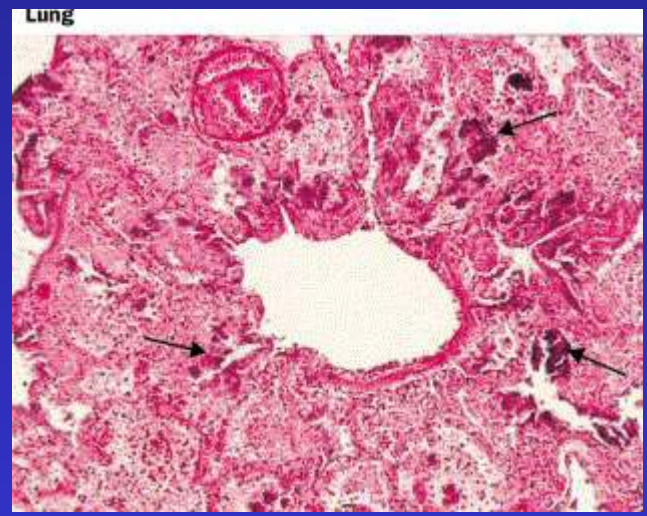


Table 1. Distribution of virulence and resistance determinants in 117 CA-MRSA isolates from three continents

Genes[b]	CA-MRSA isolates from France-Switzerland[c] n=67 (%)	USA n=29 (%)	USA n=4 (%)	Oceania[d] Southwest Pacific clone n=13 (%)	Australia Queensland clone n=4 (%)	Total n=117 (%)
Sequence type	80	1	59 or 8	30	93	
PFGE pattern	A1-7	B1-5	D1 & F1	C1-3	E1	
agr type	3	3	1	3	3	
SCC 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)
lukE-lukD	67 (100)	29 (100)	3 (75)	13 (100)	0 (0)	116 (99)
Hemolysins[e]						
hlg	0 (0)	0 (0)	0 (0)	13 (100)	0 (0)	13 (11)
hlg-v	67 (100)	29 (100)	4 (100)	0 (0)	0 (0)	100 (85)
hlb	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	1 (1)
Enterotoxins *sea*	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)
egc[f]	0 (0)	0 (0)	0 (0)	13 (100)	0 (0)	13 (11)

[a]PFGE, pulsed-field gel electrophoresis; PVL, Panton-Valentine leukocidin.

Vandenesch F. et al. Emerging Infectious Diseases 2003: 9

Community-acquired MRSA in Belgium

ULB- MRSA reference lab data 13/10/04

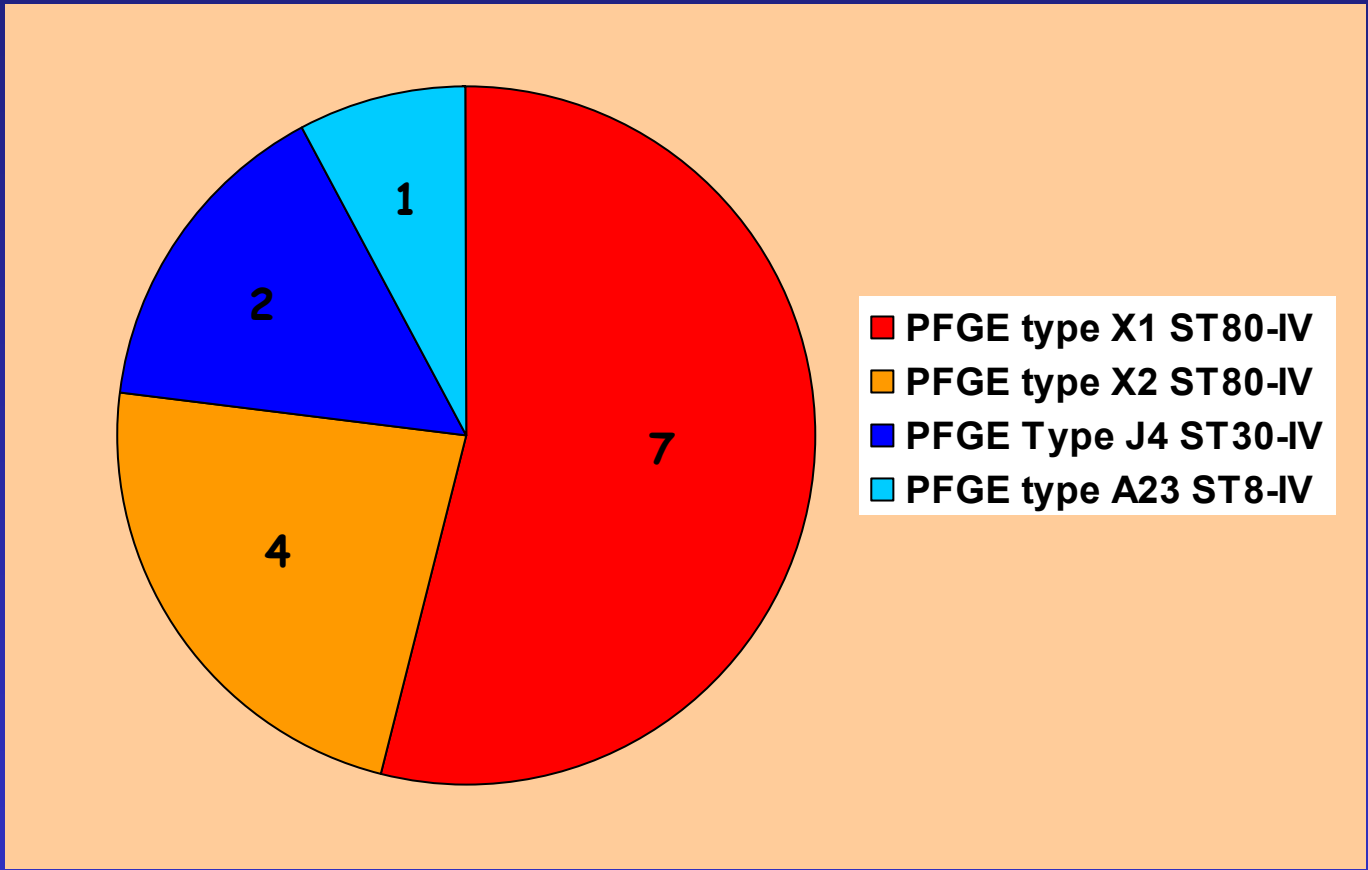
- 72 MRSA isolates from 2002 to 2004
- PCR for *luks-PV* and *lukF-PV* genes
- Susceptibility by disk diffusion method for 16 antimicrobials
- Molecular typing by PFGE, *SCCmec* and MLST

Characteristics of 15 patients with PVL (+) MRSA strains, Belgium

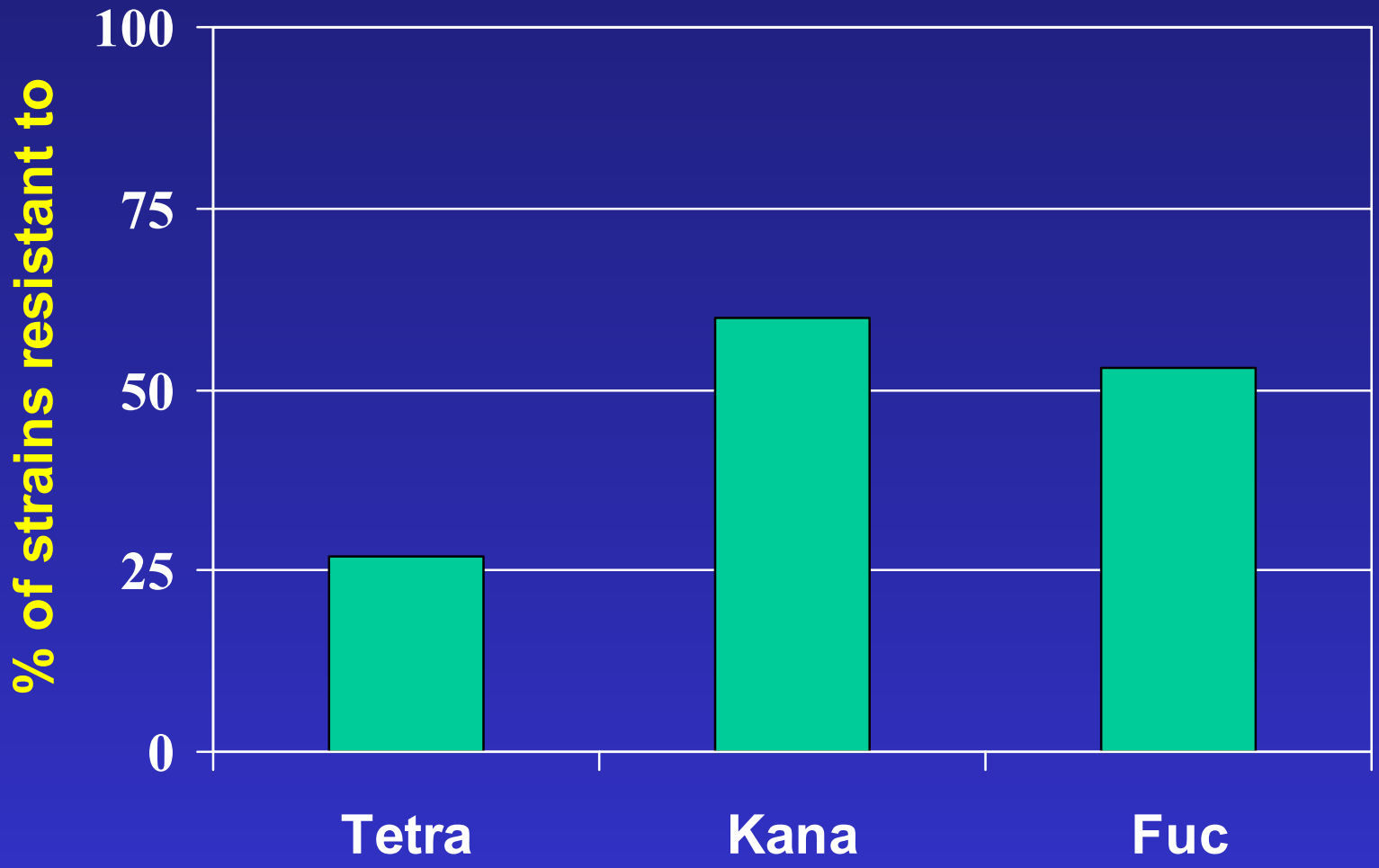
Age, mean years (range)	26 (1-70)
Sex	
Male	7
Female	7
Acquisition	
Hospital	1
Community	13
Travel abroad	3
Infection	
Cutaneous (abcess, cellulitis, furonculosis, …)	14
Bacteremia and pleuro-pneumonia	1
Peritonitis	1
Previous beta-lactam therapy	5

Strain	Antimicrobial resistance	PFGE Type	SCCmec Type	Sequence Type
1	P, OX, K, TET, FU	X1	IV	80
2	P, OX, K, TET	X1	IV	80
3	P, OX	J4	IV	30
4	P, OX, TET	A23	IV	8
5	P, OX, FU	X1	IV	80
6	P, OX, K	X1	IV	80
7	P, OX, K, TET, FU	X1	IV	80
8	P, OX	X1	IV	80
9	P, OX, TET, FU	X2	IV	80
10	P, OX, TET, FU	X2	IV	80
11	P, OX, TET	Y	ND	ND
12	P, OX, TET, FU	X2	IV	80
13	P, OX	J4	IV	30
14	P, OX, TET, FU	X1	IV	80
15	P, OX, FUC	X2	IV	80

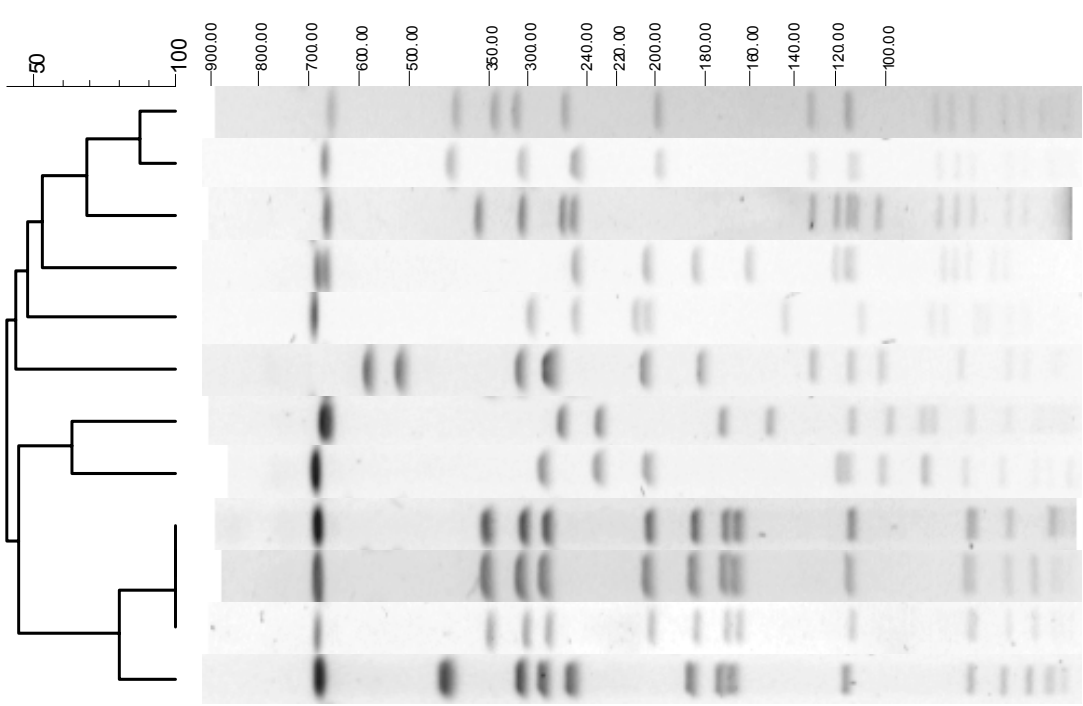
Clonal distribution of PVL positive MRSA strains (n = 14), Belgium, 2002-2004



Proportion of PVL positive MRSA strains resistant, Belgium, 2001-2003



Comparison of of community-acquired and nosocomial MRSA in Belgium: PFGE, SCCmec, MLST and PVL toxin



PFGE	SCC*mec*	ST	PVL
A1	Ia	247	Neg
A20	IV	8	Neg
A23	IV	8	Pos
L1	IV	22	Neg
B2	IV	45	Neg
G10	II	5	Neg
J4	IV	30	Pos
J1	II	36	Neg
X1	IV	80	Pos
X1	IV	80	Pos
X1	IV	80	Pos
X2	IV	80	Pos

Vandenesch et al EID 2003
Aires de Sousa et al. JCM 2003:3806
Witte et al. Eurosurveillance 2004

Conclusions

- Diversification of nosocomial epidemic MRSA clones in Belgian hospitals :
  - Decreasing prevalence of epidemic multi-resistant clone A1 ST247-MRSA-Ia
  - Emergence and spread of new epidemic clones (genta-S; *SCCmec* IV)
  - Introduction of UK EMRSA 15, 16 and New York-Japan clones ?

Conclusions

- Emergence of CA-MRSA harbouring PVL toxin genes in Belgium since 2002; minority of cases are travel-associated
- Associated with cutaneous infections or more rarely systemic/pulmonary infection
- Belonging to 3 different ST clones, 2 of which are distinct from nosocomial MRSA