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Epidemiology of methicillin-resistant *Staphylococcus aureus*: results of a nation-wide survey in Switzerland

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Summary

Objective: To assess the epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA) in Switzerland.

Material and methods: One-year national survey of all MRSA cases detected in a large sample of Swiss healthcare institutions (HCI). Analysis of epidemiological and molecular typing data (PFGE) of MRSA strains.

Results: During 1997, 385 cases of MRSA were recorded in the 5 university hospitals, in 33 acute care community hospitals, and 14 rehabilitation or long-term care institutions. Half of the cases were found at the University of Geneva Hospitals where MRSA was already known to be endemic (41.1 cases/10,000 admissions). The remaining cases (200) were distributed throughout Switzerland. The highest rates (>100 cases/10,000 admissions) were reported from non-acute care institutions. Rates ranged from 3.3 to 41.1 cases/10,000 admissions for university hospitals (mean 15.5); 0.67 to 90.4 for community hospitals (mean 4.8), and 28.2 to 315 for non-acute care institutions reporting MRSA (mean 85.7). Forty percent of MRSA patients were infected, while 60% were only colonised. The leading infection sites were skin and soft tissue (21%), surgical site (15%), and the urinary tract (26%). Whereas in Eastern Swiss HCI most MRSA cases occurred in acute care hospitals (n = 47, 98%), rehabilitation and long-term care institutions accounted for an important number of the identified cases (n = 107, 38%) in Western Switzerland.

Conclusion: Low rates of MRSA were still observed in Swiss HCI, despite one outlying acute care centre with endemic MRSA and some non-acute care institutions with epidemic MRSA. Rehabilitation and long-term care institutions contributed to a substantial proportion of cases in Western Switzerland and may constitute a significant reservoir. Overall, a national approach to surveillance and control of MRSA is mandatory in order to preserve a still favourable situation, and to decrease the risk of epidemic MRSA dissemination.

Key words: methicilin-resistant Staphylococcus aureus; epidemiology; national survey

Introduction

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is often resistant to most other antibiotics, frequently causes nosocomial infections, and is one of the greatest challenges for modern antimicrobial therapy, particularly since the emergence of *S. aureus* with intermediate susceptibility to glycopeptides [1]. In the early 1990s, a European survey indicated that MRSA tended to be more frequent in southern than in northern Europe. In countries such as France, Spain, and Italy more than 30% of *S. aureus* isolates were resistant to methicillin [2]. This was further confirmed in a more

recent survey [3]. However, within a country, MRSA prevalence may vary substantially from one hospital to another [4].

Although the reported proportion of MRSA among all *S. aureus* isolates in countries surrounding Switzerland is high, low rates (0 to 4%) have been reported in Swiss hospitals [5, 6], with the exception of the University of Geneva Hospitals (HUG) (20%) [7]. The objective of the present study was to establish a comprehensive picture of the epidemiology of MRSA in Switzerland by performing an extensive one-year survey.

Material and methods

General setting and organisation of the survey

In Switzerland, there are 5 university hospitals for a country of approximately 7 million inhabitants. In 1997, these centres organised a national survey of MRSA and collected data and isolates not only from their own hospital but, also, from other Health Care Institutions (HCI) in their region that agreed to participate. In 1997, 445 HCI were members of the H+ organisation (H+ The Swiss Hospitals, Aarau, Switzerland), which represent 80–90% of all Swiss HCI, without the nursing homes.

MRSA detection and control measures at the hospital level

Surveillance screening and control measures used in the participating institutions were standardised for the purpose of the study [6]. In brief, patients with MRSA were identified by surveillance of microbiological laboratory data from clinical specimens as well as by cultures obtained from roommates of patients infected or colonised with MRSA. When a cluster was suspected, patients of the concerned ward were screened. In addition, surveillance cultures were performed on readmission of patients previously known to have been positive for MRSA and on patients transferred from foreign hospitals. At HUG, an automatic alert system allowed immediate recognition and admission screening of patients previously know as MRSA carriers [8]. Cultured sites included anterior nares, perineal (or perirectal), and any infected sites such as open wounds.

A standard isolation procedure was applied to all patients positive for MRSA. The decolonisation procedure consisted of the application of nasal mupirocin (Bactroban®) twice daily for 5 days, associated with a daily body wash with a chlorhexidine-containing soap for 7 to 10 days. Isolation was stopped when decolonisation was documented by two sets of negative surveillance cultures obtained at least 48 h apart. Patients with infections received appropriate antibiotic therapy.

Bacterial isolates

MRSA isolates were collected by the laboratories of the university centres. Identification of *S. aureus* was confirmed by standard methods and susceptibility testing was performed by disk diffusion on Mueller-Hinton agar with 24-h incubation at 35 °C. Interpretation criteria were those of the National Committee for Clinical Laboratory Standards (NCCLS) [9]. Resistance to oxacillin was confirmed by the screen agar test [10] and on random isolates by amplification of the *mec*A gene.

Epidemiological data and definitions

A case was defined as a hospitalised patient found to be infected or colonised with MRSA during the study period. For each case, the following characteristics and risk factors for MRSA colonisation/infection were recorded: demographic data, geographic origin, admission and discharge dates, prior hospitalisation during the preceding 3 years, past history of MRSA colonisation or infection, presence of comorbidities (Charlson score [11]), functional status (Karnofsky index [12]), underlying diagnosis, infection versus colonisation with MRSA, presence of indwelling urinary or vascular catheter, wound, drains, endotracheal tube, antibiotic treatment and operation.

Cases considered as having acquired MRSA before admission (pre-hospitalisation acquisition) were: (1) patients known to have been colonised/infected with MRSA during a prior hospitalisation; (2) cases with MRSA detected within 72 h of admission; and (3) cases where the isolate exhibited a PFGE pattern observed only once (unique) in a given hospital (thus presumed to have been introduced by the patient). Other cases were considered as newly hospital-acquired MRSA.

Standard definitions for nosocomial infections of the Centers for Diseases Control and Prevention (CDC) were used [13]. A case was considered infected by MRSA (as opposed to colonised) when MRSA was isolated from a sterile site, or when signs of infection motivated systemic antibiotic therapy and/or surgical procedure.

Results

General data

From January to December 1997, 385 cases of MRSA were identified and reported from the 5 university hospitals, 33 other acute care hospitals, and 14 rehabilitation or long-term care institutions throughout the country (table 2, figure 1). Ten additional HCI reported not to have observed any MRSA cases. Both epidemiological data and isolates were available for 225 (63%) of the cases, whereas only epidemiological data or isolates were available for 97 and 63 cases, respectively.

Demographic and clinical characteristics of the MRSA cases are shown in table 1. Variations in the origin of the patients between institutions were observed (table 2). Although 52% of the patients were admitted from their home 92% had been hospitalised in the previous 3 years. Transfer from another hospital (within or outside Switzerland) was the next most frequent origin of cases.

Table 1

Demographic and clinical characteristics of the MRSA cases.

Mean age (range)	66 (0–99)
Sex (male)	212/376 (57%)
Presence of comorbidities	199/276 (72%)
Indwelling urinary catheter	98/267 (37%)
Vascular catheter	159/269 (59%)
Wounds	130/211 (62%)
Drains	31/262 (12%)
Endotracheal tube	48/265 (18%)
Operation	70/264 (17%)
Antibiotic treatment	177/245 (72%)
Haemodialysis	1/284 (0.3%)

MRSA rates

The proportions of MRSA among all *S. aureus* isolates were 4, 3, 23, 3, and 6% in Basel, Bern, Geneva, Lausanne, and Zurich university hospitals, respectively. The highest number of MRSA cases/10,000 admissions in a university hospital was found at HUG (41.1), whereas it was below 10/10,000 admissions in the other university hospitals (table 2). The mean rate was 4.8 cases/10,000 admissions in acute community hospitals (range 0.67 to 90.4) and 85.7/10,000 admissions in rehabilitation and long-term care institutions that reported MRSA cases (range 28.2 to 315). The incidence-density of all MRSA cases averaged 0.93/10,000 patient-days, and varied from 0.2 to 2.1 in university hospitals (mean 1.2), from 0.06 to 3.0 (mean 0.47) in other acute care hospitals, and from 0.6 to 13.5 (mean, 2.2) in rehabilitation or long-term care institutions.

Table 2

Incidence and demographic characteristics of MRSA cases.

	University hospitals					Other health care institutions		Total
	Basel	Bern	Geneva	Lausanne	Zurich	acute care (N = 25)	non acute care (N = 14)	
No. of cases	8	12	185	24	18	85	53	385
Origin[1,2] (%):						N = 33	N = 16	N = 296
home	5 (71%)	3 (25%)	103 (79%)	11 (46%)	5 (28%)	16 (49%)	10 (41%)	153 (52%)
nursing home	0	0	6 (5%)	2 (8%)	2 (11%)	9 (27%)	2 (20%)	21 (7%)
transfer from Swiss hospital	1 (14%)	2 (17%)	7 (5%)	4 (17%)	4 (22%)	7 (21%)	4 (37%)	29 (10%)
transfer from a hospital outside Switzerland	1 (14%)	6 (50%)	9 (7%)	7 (29%)	6 (33%)	0	0	29 (10%)
other origin	0	1 (8%)	6 (5%)	0	0	1 (3%)	0	8 (3%)
Prior hospitalisation[2]	8/8 (100%)	9/10 (90%)	169/184 (92%)	23/24 (96%)	15/16 (94%)	26/30 (87%)	14/15 (93%)	264/287 (92%)
No. of cases / 10'000 adm.[2]	3.5	3.3	41.1	9.3	6.1	4.8	85.7	10.6
No. of cases / 10'000 patient-days[2]	0.24	0.37	2.1	1.15	0.79	0.47	2.2	0.93
No. of infections/ 10'000 admissions[2]	0.4	1.4	13.8	1.6	2.7	n.a.	n.a.	n.a.

[1] during the previous 3 years.
[2] for cases for whom data was known.
n.a., not available

Figure 1

A. Geographical distribution of MRSA cases in Switzerland, 1997. Each circle represents one institution, the number in the circle is the number of MRSA cases reported for this institution.

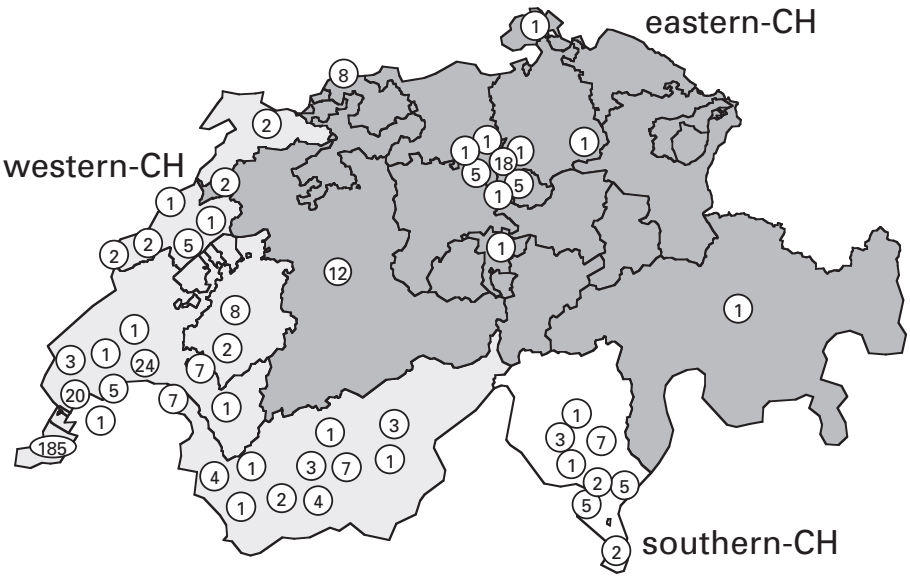


Table 3

Proportions (in %) of MRSA cases in the different wards of acute institutions in each geographical region (HUG, and other hospitals of Western Switzerland and Eastern Switzerland; data not available for Southern Switzerland).

Wards	HUG N = 126	Western CH N = 56	Eastern CH N = 47	Total N = 229
Acute				
Emergency	0	17.8	8.5	6.1
ICU	4.8	7.1	21.3	8.7
Medicine	50.8	37.5	21.3	41.5
Surgery	34.1	26.8	25.5	30.6
Paediatrics	6.3	5.4	6.4	6.1
Other	4.0	5.4	17.0	7.0
Total	100	100	100	100

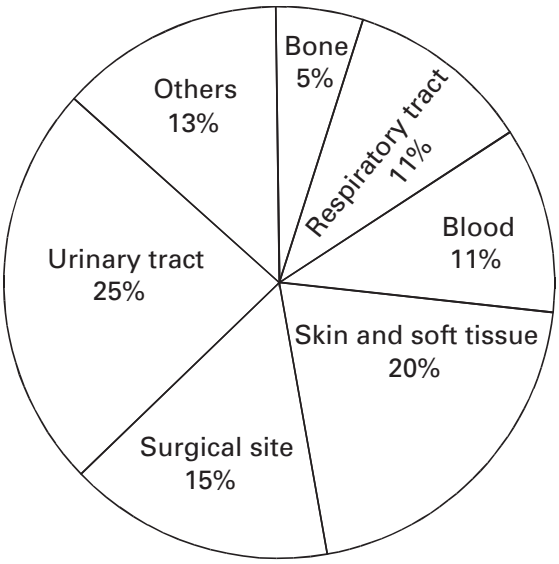
Table 4

Proportions (%) of MRSA cases in the different institutions of each geographical region: Geneva area, Western Switzerland (Geneva excluded), Eastern and Southern Switzerland.

	Geneva area N = 178	Western CH N = 113	Eastern CH N = 59	Southern CH N = 25
Acute				
University hospitals	76.4	21.2	67.8	
Community hospitals				
>500 beds			10.1	
250–499 beds		15.0	5.0	24
125–244		11.5	11.9	36
<125		14.2	3.4	40
Non acute				
Rehabilitation	23.6	28.3		
Long-term care		9.7	1.7	
Total	100	100	100	100

Figure 2

Frequency of MRSA infection sites (N = 138).



Hospitalisation ward

Table 3 shows the wards on which patients were hospitalised at time of detection. Most cases (72%) occurred in medical or surgical units. MRSA observed in intensive care units (ICUs) represented less than 8% of cases in Western Swiss hospitals whereas, in Eastern Switzerland, they accounted for 21%. Of note, among the 20 cases which occurred in Swiss ICUs, 9 (45%) were transferred from foreign hospitals.

Type of institution

The distribution of cases according to the type of institution (acute hospitals of various sizes, rehabilitation, and long-term care facilities) is shown in table 4. In Western Swiss HCI, between 24 and 39% of cases were observed in non-acute care institutions (rehabilitation and long-term care facilities) whereas this proportion was below 2% in Eastern and Southern Switzerland. Analysis of molecular data showed that 86% (48/56) of cases in non-acute care wards of Western Switzerland were due to an epidemic clone. By comparison, this clone accounted for only 40% (19/47) of the cases observed in acute care hospitals.

Prior versus new acquisition of MRSA

For the university hospitals, the epidemiological data permitted determination of whether MRSA had most likely been acquired before (= prior acquisition) or during the hospitalisation considered in the study (= new acquisition) (table 5). Overall, 86/309 (28%) cases were considered to have been newly-acquired MRSA. The rates varied from 8.3 to 29% between the different university hospitals. Based on this data, the attack rate of MRSA, defined as the number of newly-acquired MRSA while admitted to the different university hospitals, averaged 2.8 ranging from 0.3 to 8.1 cases/10,000 admissions.

Among the 144 cases with prior acquisition of MRSA and for which data were available, 94 (65%) came from home, 36 (25%) were transferred from Swiss (7%) or foreign (18%) hospitals, and 9 (6%) from non-acute care institutions. Among patients admitted directly from home, 92% of cases had been hospitalised previously (table 2).

MRSA infections

Overall, 116/291 (40%) of cases were considered as having clinical infections with a total of 138 infections. Infection rates ranged from 0.4 to 13.8/10,000 admissions in university hospitals

Table 5

Prior versus new acquisition of MRSA in the different university hospitals.

	Basel	Bern	Geneva	Lausanne	Zurich	Total
Prior acquisition (n)	5	11	129	19	15	179
New acquisition (n)	2	1	31	5	3	42
Undetermined[1] (n)	1	0	25	0	0	26
New / [prior + new] (%)	29%	8.3%	19%	21%	17%	19%
No. new /10,000 admissions	0.9	0.3	8.1	1.9	1.0	2.8

[1] no data available

(table 2). Data were not available for most other HCI. The leading infection sites were the urinary tract (25%), skin and soft tissue (20%) and the surgical site (15%) (figure 2). No significant difference in the distribution of the sites of infection was observed between the different hospitals.

Molecular epidemiology

Molecular typing (pulsed field gel electrophoresis) was performed on isolates of 288/385 of the cases (one isolate per case). Detailed results have been published elsewhere [25]. Results showed that 65% of the isolates belonged to four predominant clones, three of which were mostly present in Geneva hospitals (figures 3 and 4). The remaining 35% of the isolates were clustered into 67 genotypes and they accounted for 1 to 5 patients per hospital (figure 3).

Figure 3

Distribution of genotypes in community and university (Basel, Bern, Geneva, Lausanne and Zurich) hospitals (one strain per case). The four predominant clones (WCH, GE1, GE2 and GE3) are represented by their major type (1, 9, 40 and 57, respectively) and their subtypes (letters). Reproduced with the permission of Clinical Microbiology and Infection [25].

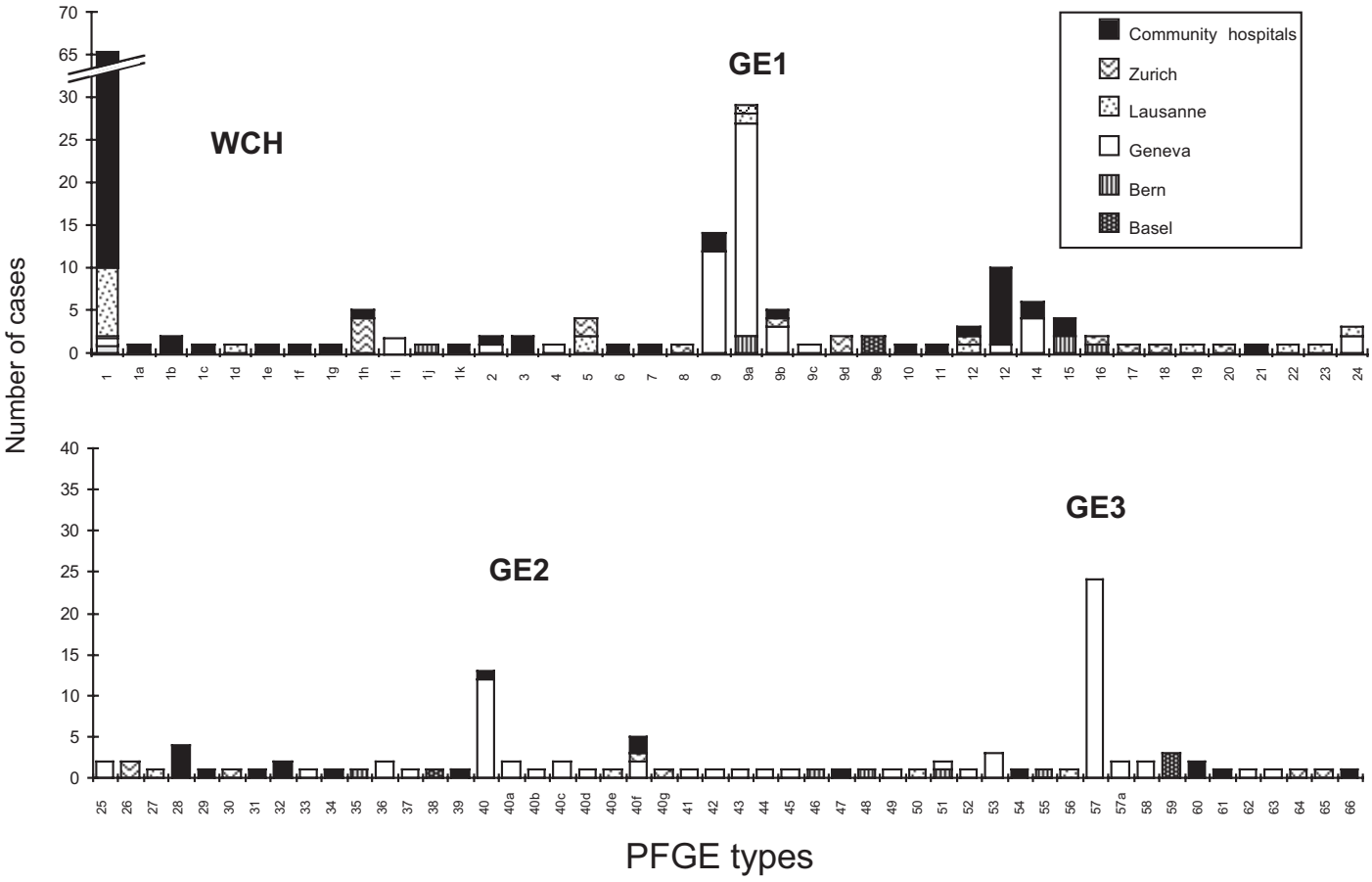
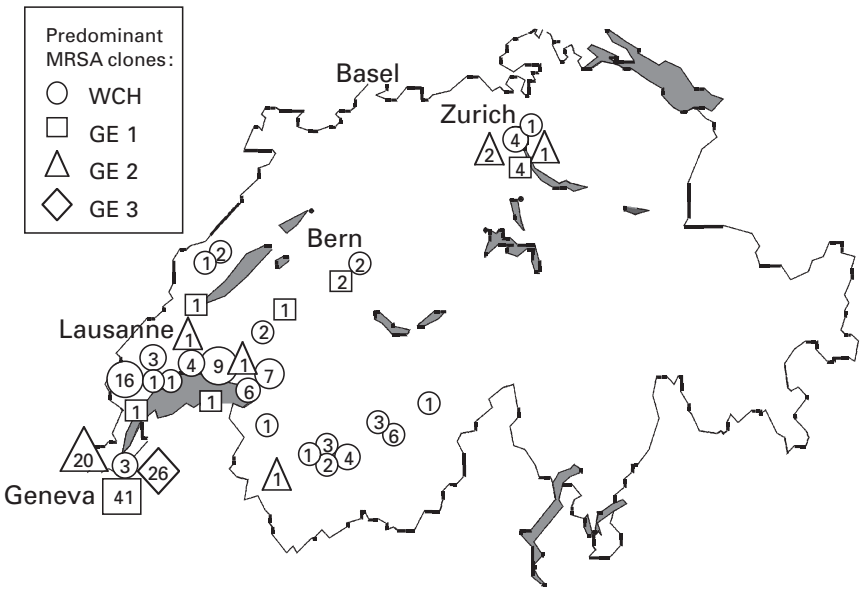


Figure 4

Geographical distribution of the four predominant clones of MRSA in Switzerland in 1997 (one symbol per institution and per clone, the number in the symbol indicates the number of cases harbouring the clone in the institution). Reproduced with the permission of Clinical Microbiology and Infection [25].



Discussion

This study is the first nationwide survey on MRSA carried out in Switzerland. The results confirm that Swiss HCI have a low prevalence of MRSA, with the exception of the HUG and some non-acute care institutions in the western part of the country [8, 14].

Although a substantial number of institutions participated in the study, our results are derived from a convenience sample of hospitals that volunteered to participate, and cannot be extrapolated to the whole of Switzerland for two reasons. First, university hospitals which have all participated in the study, represent a non-negligible bias since risk factors for MRSA are much higher in this type of institution. Second, although we received data from 10 community hospitals reporting no MRSA during the period of the survey, we had no data from the other Swiss healthcare centres. However, regarding the relatively low number of MRSA cases recovered in most of the reporting institutions and taking into account the tight network among Swiss infection control practitioners, it is unlikely that non-reporting institutions have experienced a substantial MRSA burden.

Different methods of calculation can be used to measure the magnitude of MRSA occurrence at a particular institution. The least informative figure, but also the most frequently reported as it is the easiest to obtain and relies only on microbiology laboratory data, is the proportion of MRSA among all *S. aureus* isolates in an institution. This proportion allows a rough comparison between hospitals, although it also requires precise definitions (eg, one isolate per patient). Thus, the HUG, with 23%, have a rate comparable to hospitals of countries surrounding the southern part of Switzerland [2, 15–17]. The other Swiss institutions showed proportions below 5%, figures which are comparable to northern European hospitals such as those in Germany [2], the Netherlands [2, 18, 19], Denmark [2] or in Sweden [2, 20]. In Germany, an increase of the proportion of *S. aureus* strains resistant to methicillin from 1.7% to 12.9% has been reported between 1990 and 1995 [21].

The number of infected or colonised MRSA cases/10,000 admissions, or the number of MRSA infections/10,000 admissions provide more appropriate figures for comparison between institutions or for longitudinal surveillance. With 0.4 to 2.7 MRSA infections/10,000 admissions, our study shows that university hospitals in Switzerland currently have a low incidence of MRSA, with the exception of HUG where a rate of 13.8 infections/10,000 admissions was reported. By comparison, MRSA-infected patients/10,000 admissions in 43 French hospitals were recently estimated to range between 18 to 158 [22]. It was estimated at 165/10,000 admissions in Irish hospitals [23]. The incidence density (number of cases per patient-day) may be the best indicator for comparison between institutions. Indeed, in the present study, the incidence seems quite high in long-term care institutions when using the number of cases/10'000 admissions, but is much more comparable to university hospitals when looking at the incidence density (patients stay longer in long-term care hospitals, therefore there are fewer admissions for more patient-days of stay).

The study also shows that the epidemiology of MRSA in Switzerland differs from one region to another. The highest reported incidences of MRSA cases (>100 cases/10,000 admissions) was reported from non-acute care institutions (rehabilitation and long-term care), in particular in the western part of the country. Importantly, whereas the high number of cases of Western Switzerland were reported from the non-acute institutions, these institutions did not seem to play a major role in Eastern and Southern Switzerland. A recruitment bias between Western and Eastern Switzerland can, nevertheless, not be excluded. As the majority of the cases in non-acute care institutions were due to an epidemic clone [24], these institutions probably played an important role in the dissemination of the clone, as transfers of patients from and to acute care hospitals are frequent. These institutions might serve as a reservoir for MRSA and infection control strategies are mandatory to limit the spread of the MRSA within these HCI and reduce MRSA transfer to others.

Owing to a higher prevalence of MRSA in HUG, one aim of this study was to establish to what extent this potential reservoir could spread to other western institutions in Switzerland. Part of the answer is given by the results of molecular typing of these isolates [25] which showed that: (1) 3 clones are responsible for the majority (73%) of the cases at HUG; (2) these clones were rarely observed in other hospitals; and (3) the majority of the cases in the western part of Switzerland, excluding Geneva, was due to a fourth epidemic clone [24]. Thus, it seems that HUG faced mainly a geographically-limited problem which did not extend to the rest of Switzerland. As described for Western Switzerland, non-acute care beds were responsible for a large proportion of MRSA cases at HUG.

An important finding of the present study was that MRSA cases in ICUs accounted for less than 9% of all cases, as compared with other European hospitals where the majority of cases are observed in these units. However, the proportion was somewhat higher in the eastern part of Switzerland. Another important finding is the fact that in university hospitals, less than 30% of cases can be considered as having acquired their MRSA during the hospitalisation, the remaining 70% being probably acquired during previous hospital stays. Finally, the attack rate of MRSA transmission, which could only be assessed appropriately in university

hospitals, remains extremely low in Switzerland with an average incidence of 2.8 cases/10,000 admissions. This illustrates the efficacy of infection control programs, even in hospitals with high endemicity or surrounded by known acute care facilities with extremely high numbers of MRSA patients, probably resulting from an ongoing outbreak.

In conclusion, the study confirms and extends previous data and shows that most Swiss hospitals have a low incidence of MRSA, despite some outlying institutions with endemic or highly epidemic MRSA conditions and neighbouring countries with a high prevalence. This might be the result of an "aggressive" policy of MRSA surveillance and control [6, 14]. Overall, a national approach to surveillance and control of MRSA is warranted in Switzerland in order to prevent conditions arising which favour its further development, thereby decreasing the risk of epidemic MRSA transmission.

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References

1 Hiramatsu K, Aritaka N, Hanaki H, et al. Dissemination in Japanese hospitals of strains of *Staphylococcus aureus* heterogeneously resistant to vancomycin. Lancet 1997;350:1670–3.
2 Voss A, Milatovic D, Wallrauch-Schwarz C, et al. Methicillin-resistant *Staphylococcus aureus* in Europe. Eur J Clin Microbiol Infect Dis 1994;13:50–5.
3 Veldhuijzen I, Bronzwaer S, Degener J, et al. European antimicrobial resistance surveillance system (EARSS): susceptibility testing of invasive *Staphylococcus aureus*. Euro Surveillance 2000;5:34–6.
4 Struelens MJ, Mertens R, and Groupement pour le Dépistage lelPdIH. National Survey of methicillin-resistant *Staphylococcus aureus* in Belgian hospitals: detection methods, prevalence trends and infections control measures. Eur J Clin Microbiol Infect Dis 1994;13:56–63.
5 Lugeon C, Blanc DS, Wenger W, et al. Molecular epidemiology of methicillin-resistant *Staphylococcus aureus* at a low incidence hospital over a 4-year period. Infect Control Hosp Epidemiol 1995;16:260–7.
6 Francioli P, Furrer H, Pittet D, et al. Staphylocoques dorés résistants à la méthicilline: situation et enjeux. Swiss-Noso 1995; 4:25–29.
7 Harbarth S, Romand J, Frei R, et al. Transmission inter- et intrahospitalière de staphylocoques dorés résistants à la méticilline. Schweiz Med Wochenschr 1997;127:471–8.
8 Pittet D, Safran E, Harbarth S, et al. Automatic alerts for methicillin-resistant *Staphylococcus aureus* surveillance and control: role of a hospital information system. Infect Control Hosp Epidemiol 1996;17:496–502.
9 Jorgensen JH, Cleeland R, Craig W, Doern G, Ferraro MJ, Finegold SM, Hansen SL, Jones RN, Pfaller MA, Preston DA, Reller LB, Swenson JM, Waitz JA. Performance standards for antimicrobial disk susceptibility testing. Approved Standard M2-A4. National Committee for Clinical Laboratory Standards. 1991.
10 In: Isenberg HD, ed. Essential procedures for clinical microbiology. Washington: ASM 1998.
11 Wilson WR, Karchmer AW, Dajani AS, et al. Antibiotic Treatment of adults with infective endocarditis due to streptococci, enterococci, staphylococci, and HACEK microorganisms. JAMA 1995;274:1706–13.
12 Karnofsky DA, Burchenal JH. The clinical evaluation of chemotherapeutic agents in cancer. In: MacLeod CM, ed. Evaluation of chemotherapeutic agents. New York, NY: Columbia University Press, 1949:191–205.
13 Pittet D, Harbarth S, Ruef C, et al. Prevalence and risk factors for nosocomial infections in four university hospitals in Switzerland. Infect Control Hosp Epidemiol 1999;20:37–42.
14 Harbarth S, Martin Y, Rohner P, et al. Effect of delayed infection control measures on a hospital outbreak of methicillin-resistant *Staphylococcus aureus*. J Hosp Infect 2000;46:43–9.
15 Struelens MJ, Ronveaux O, Jans B, et al. Methicillin-resistant *Staphylococcus aureus* epidemiology and control in Belgian hospitals, 1991 to 1995. Groupement pour le Depistage, l'Etude et la Prévention des Infections Hospitalières. Infect Control Hosp Epidemiol 1996;17:503–8.
16 Melo-Cristino J. Antimicrobial resistance in staphylococci and enterococci in 10 Portuguese hospitals in 1996 and 1997. POSGAR. Portuguese Study Group of Antimicrobial Resistance. Microb Drug Resist 1998;4:319–24.
17 Richet H, Wiesel M, Le Gallou F, et al. Methicillin-resistant *Staphylococcus aureus* control in hospitals: the French experience. Association des Pays de la Loire pour l'Eviction des Infections Nosocomiales. Infect Control Hosp Epidemiol 1996; 17:509–11.
18 Vandenbroucke-Grauls CM, Frenay HM, van Klingeren B, et al. Control of epidemic methicillin-resistant *Staphylococcus aureus* in a Dutch university hospital. Eur J Clin Microbiol Infect Dis 1991;10:6–11.
19 Vandenbroucke-Grauls CM. Methicillin-resistant *Staphylococcus aureus* control in hospitals: the Dutch experience. Infect Control Hosp Epidemiol 1996;17:512–3.
20 Seeberg S and Larsson L. [Methicillin resistant *Staphylococcus aureus*. A problem also in Sweden]. Lakartidningen 10.9.1997; 94:3174–6, 3179.
21 Witte W, Kresken M, Braulke C, et al. Increasing incidence and widespread dissemination of methicillin-resistant *Staphylococcus aureus* in hospitals in central Europe, with special reference to German hospitals. Clinical Microbiology and Infection 1997; 3:414–22.
22 Methicillin-resistant *Staphylococcus aureus* in French hospitals: A 2-month survey in 43 hospitals, 1995. The Hopital Propre II Study Group. Infect Control Hosp Epidemiol 1999;20:478–86.
23 Johnson Z, Fitzpatrick P, Hayes C, et al. National survey of MRSA: Ireland, 1995. J Hosp Infect 1997;35(3):175–84.
24 Blanc DS, Petignat C, Moreillon P, et al. Unusual spread of a penicillin-susceptible methicillin-resistant *Staphylococcus aureus* clone in a geographic area of low incidence. Clin Inf Dis 1999;29:1512–8.
25 Blanc DS, Pittet D, Ruef C, et al. Molecular epidemiology of predominant clones and sporadic strains of methicillin resistant *Staphylococcus aureus* in Switzerland and comparison with European epidemic clones. Clin Microbiol Infect 2002; In press.

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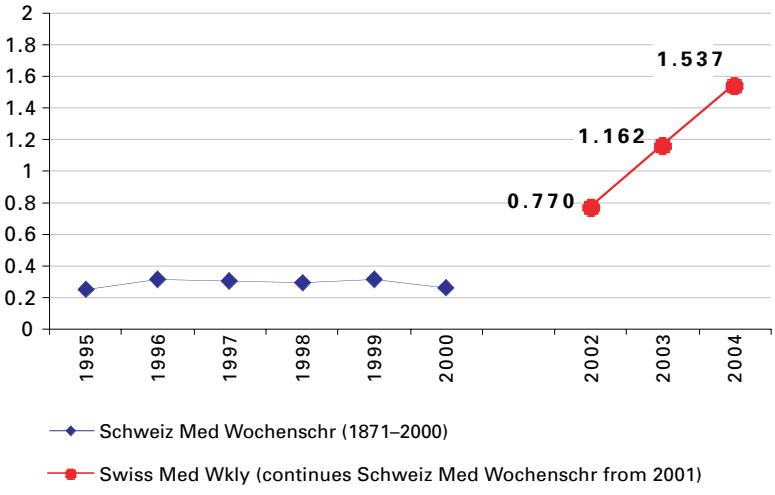

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