Curbing Methicillin-Resistant *Staphylococcus aureus* in 38 French Hospitals Through a 15-Year Institutional Control Program

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**Background:** The Assistance Publique–Hôpitaux de Paris (AP-HP) institution administers 38 teaching hospitals (23 acute care and 15 rehabilitation and long-term care hospitals; total, 23 000 beds) scattered across Paris and surrounding suburbs in France. In the late 1980s, the proportion of methicillin resistance among clinical strains of *Staphylococcus aureus* (MRSA) reached approximately 40% at AP-HP.

**Methods:** A program aimed at curbing the MRSA burden was launched in 1993, based on passive and active surveillance, barrier precautions, training, and feedback. This program, supported by the strong commitment of the institution, was reinforced in 2001 by a campaign promoting the use of alcohol-based hand-rub solutions. An observational study on MRSA rate was prospectively carried out from 1993 onwards.

**Results:** There was a significant progressive decrease in MRSA burden (~35%) from 1993 to 2007, whether recorded as the proportion (expressed as percentage) of MRSA among *S aureus* strains (41.0% down to 26.6% overall; 45.3% to 24.2% in blood cultures) or incidence of MRSA cases (0.86 down to 0.56 per 1000 hospital days). The MRSA burden decreased more markedly in intensive care units (~59%) than in surgical (~44%) and medical (~32%) wards. The use of ABHR solutions (in liters per 1000 hospital days) increased steadily from 2 Lt to 2.1Lt in acute care hospitals and to 10 L in rehabilitation and long-term care hospitals following the campaign.

**Conclusion:** A sustained reduction of MRSA burden can be obtained at the scale of a large hospital institution with high endemic MRSA rates, providing that an intensive program is maintained for a long period.

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**Methods**

**Setting**

The AP-HP is a public institution that administers 38 teaching hospitals (23 acute care hospitals [ACHs] and 15 rehabilitation and long-term care hospitals [RLTCHs]) scattered across Paris (n = 13) and surrounding suburban counties.
MRSA CONTROL PROGRAM

A program aimed at controlling MRSA was launched in 1993, based on the following objectives:

1. **Isolation Interventions:** (1) Placement of patients with MRSA infections or colonizations in single-bed rooms whenever possible and (2) barrier precautions for patients with MRSA infections or colonizations such as disposable gloves worn before and discarded after patient contact, disposable aprons worn for extensive contacts (eg, bed making), and small equipment (eg, stethoscope) dedicated to the patient.

2. **Promotion of Hand Hygiene:** (1) Hand washing with disinfectant soap after contact with patients with MRSA infections or colonizations before leaving the room and (2) an institutional campaign for promoting the use of alcohol-based hand rub (ABHR) solutions in place of hand washing, launched in 2001 to reinforce the program, which provided pedagogical material to the infection control teams (slide shows, 200 000 brochures, and 14 000 posters) and material on training these teams and sent formal letters by the general director asking all administrators, heads of departments, and chief nurses to support the campaign.

3. **Identification of Patients With MRSA Infections or Colonizations:** (1) Passive surveillance through routine clinical specimens; (2) active surveillance (screening) by culturing nares swabs when there is a high risk of MRSA colonization, eg, intensive care unit (ICU) patients and contact patients (ie, those hospitalized in the same unit and at the time as patients with MRSA infections); (3) notification of new patients with MRSA infections or colonizations by laboratories to medical teams using quick reporting systems (eg, telephone call) and flags on laboratory reports (“watch MRSA”); (4) identification of patients with MRSA infections using a specific self-sticking label on the door to the patient’s room and medical charts; and (5) informing units to which patients with MRSA are transferred.

4. **ABHR SOLUTION USE**

Following the launch in 2001 of the ABHR campaign, the annual ABHR solution use was recorded in liters per 1000 hospital days (HDs) using the data provided by the central pharmacy.

5. **STIMULATION OF EFFORTS BY THE INSTITUTION**

Since 1998, our institution has further stimulated the efforts by asking each hospital to report annually to the central administration the following selected information on the program, as part of a wider process to promote the quality at AP-HP: (1) size of the infection control team, (2) implementation of the program, (3) organization of audits (eg, on hand hygiene), and (4) feedback. The progress of the initiative has been annually presented during meetings of infection control teams and bacteriologists from all AP-HP hospitals, yielding opportunities to discuss the results, and disseminated within each hospital and central administration.

6. **RESULTS**

**IMPLEMENTATION OF THE MRSA CONTROL PROGRAM IN AP-HP HOSPITALS**

By 1995, 16 of the 23 ACHs and 5 of the 15 RLTCHs (P=.04) had implemented the program launched in ACHs and RLTCHs, representing 36% of all the hospital beds in the Paris area (“Île de France”; 11.6 million inhabitants) and 5% of all the beds in France, and admits approximately 1 million patients per year and employs 19 000 physicians, 18 300 nurses, and 29 800 assistant nurses. AP-HP hospitals are managed locally by administrators and medical committees, but decisions on large investments and medical developments are made by the central administration. A local team is in charge of prevention and surveillance of nosocomial infections in each hospital, but actions of foremost importance for the whole institution, such as campaigns for hygiene, are coordinated centrally.
Almost all the ACHs (19 of 23), but only 7 of the 15 RLTCHs, had done so in 1996 (P = .02). Reports sent from 1998 onwards by each hospital showed that notification of patients with MRSA infections or colonizations by laboratories had been implemented in all hospitals by 1998 and that active surveillance, targeting mainly ICUs, was implemented in almost all ACHs by 1998 and in all by 1999. Screening compliance was not recorded at central level but reached approximately 80% of the targeted patients in 12 ICUs of 5 hospitals that championed the initiative. By 2001, all ACHs, but a third of RLTCHs, had organized audits (eg, on hand hygiene), following local procedures and timing. Feedback information had been formalized by all hospitals by 2001.

USE OF ABHR SOLUTION

Following the ABHR campaign, use of ABHR solution increased regularly between 2000 and 2007 (Figure 1) from 2 L to 21 L per 1000 HDs but reached a higher level in ACHs than in RLTCHs (26 L and 10 L per 1000 HDs, respectively). The proportion of MRSA among S aureus strains decreased from 39.4% in 1993 to 21.6% in 2007 in ACHs (relative change, −45%; P < .001), interrupted by a temporary rebound in 2000-2001 (Figure 2). The decrease was sharper in ICUs (from 55.1% to 22.4%; relative change, −59%; P < .001) and in surgical wards (from 38.7% to 21.7%; relative change, −44%; P < .001) than in medical wards (from 33.1% to 22.5%; relative change, −32%; P < .001) (Figure 3). The decline was significant and similar for 3 strata of ACHs (400-500, 800-1000, and >1000 beds). The decrease was also sharp in the strains isolated from blood cultures (from 45.3% to 24.2%; P < .001) and from pus and serous fluids (from 40.4% to 18.0%; P < .001).

In RLTCHs, the proportion of MRSA among S aureus strains remained high throughout the survey, ranging between 54% and 73%. As a result, the global decrease at AP-HP as a whole was less marked than in ACHs (from 41.0% in 1993 to 26.6% in 2007; relative change, −35%; P < .001).

INCIDENCE OF MRSA CASES

The incidence of MRSA cases decreased from 1.16 per 1000 HDs in 1996 to 0.57 in 2007 (relative change, −51%; P < .001) (Figure 2 and Figure 4). The decrease was sharper in ICUs (from 2.95 to 1.23 per 1000 HDs; relative change, −58%; P = .001) and in surgical wards (from 1.52 to 0.72 per 1000 HDs; −52%; P = .001) than in medical wards (from 0.70 to 0.48 per 1000 HDs; relative change, −31%; P = .04). When expressed per 100 admissions, the incidence of MRSA decreased in ACHs from 0.90 in 1996 to 0.44 in 2007 (P = .001).

In RLTCHs (Figure 4) the incidence rate initially increased from 0.49 to 0.94 per 1000 HDs between 1996 and 2001 (P = .001) and began to decrease only after 2001, down to 0.54 in 2007 (P = .001), ie, returning to the level observed in 1996. As a result, the global decrease in MRSA incidence in AP-HP as a whole was less marked than in ACHs, from 0.86 to 0.56 per 1000 HDs (relative change, −35%; P = .001).
TREND IN MRSA RATES BEFORE AND AFTER LAUNCHING THE ABHR CAMPAIGN

When introducing 2 periods (period 1, up to the ABHR campaign launch; period 2, after the campaign launch) in a multivariate model, the period was a significant variable of the decrease in MRSA incidence, but not the year, and interaction between the study period and year was established, justifying a separate analysis for each period. In ACHs, the MRSA rate decreased less sharply in period 1 (relative change, −2% per year) than in period 2 (relative change, −4.7% per year). The contrast was particularly apparent in medicine, where the percentage increased in period 1 (relative change, +2.3% per year) but decreased in period 2 (relative change, −6.2% per year). In surgery, the relative decrease was −1.8% per year in period 1 and −4.7% per year in period 2, but remained steady over both periods in ICUs.

SUSCEPTIBILITY PATTERN IN MRSA

Between 1993 and 2007, the susceptibility rates among MRSA strains significantly increased (P < .001) for gentamicin (from 12% to 95%), erythromycin (from 8% to 63%), and rifampicin (from 27% to 92%). In contrast, the susceptibility rates remained unchanged for fluoroquinolones (<10%) and fusidic acid (>85%). The proportion of MRSA strains with decreased susceptibility to vancomycin (vancomycin intermediate-resistant *S aureus*, defined as vancomycin minimum inhibitory concentration >4 mg/L) remained below 1%.

COMMENT

An MRSA control program was launched in 1993 in the 38 hospitals of the AP-HP institution in response to the results of the first European MRSA comparative study conducted in 1990 showing high rates (approximately 35% of MRSA among the clinical isolates of *S aureus*) in France, Italy, and Spain, contrasting with low rates (<2%) in northern European countries. These results triggered the decision to take prompt action in our institution. Our MRSA control program was similar to, and largely based on, the guidelines published by national agencies that were available at that time and to which few changes have been made since. The program focused on a bundle of measures aimed at decreasing cross-transmission including single room placement, promotion of hand hygiene, active surveillance in high-risk patients, quick notification of cases, and feedback. Decolonization by mupirocin was not recommended due to the risk of resistance and was used scarcely. We did not close units where MRSA rates were particularly prevalent. Controlling antibiotic use was not attempted at the institution level during the study, and the overall use of antibiotics at AP-HP remained stable at approximately 450 defined daily doses per 1000 HDs. The MRSA control program was progressively implemented at AP-HP, more readily and completely in ACHs than in RLTCHs. The campaign launched halfway through the study to promote the use of ABHR solutions whereas classic hand washing was advocated in the first phase of the study, led to a dramatic increase in ABHR solution use, sharper in ACHs than in RLTCHs.

The main result of the present study was the clear decrease in MRSA burden (−35%) between 1993 and 2007,
or transfers, often within AP-HP, and were all recorded
MRSA cases were hospital acquired, either locally or
quired MRSA”), first identified in the early 2000s in
France, was related to the rapid spread of new hospi-
susceptibility to gentamicin), already reported in
France,22 was related to the rapid spread of new hospi-
results, based on all clinical specimens and not tar-
setting. The decrease of MRSA in blood cultures (−47%)
counterbalanced the increase that initially occurred in 1993
A subset of ACHs that led the initiative and generally ap-
cline was steady and sharp in ICUs (−59%), where control
measures have been readily implemented, and to a lesser
extent in surgical wards (−44%) that are strongly con-
less marked (−32%) and was delayed until the
years of the study, there was a trend to sharper decline in
The information is presented as follows: name of hospital (name of the head of laboratory/name[s] of the corresponding
Study and Group Information
AP-HP Hospitals, Heads of Laboratories of Bacteriology, Corresponding Members of the Collègiale
de Bactériologie-Virologie-Hygiène des Hôpitaux Universitaires de l’Ile-de-France,
and Heads of the Infection Control Teams
The major limitation of our study is its observational
design and lack of a control group. Indeed, the aim was
to curb as quickly as possible the high MRSA rates pre-
vailing in the early 1990s, and the study was conducted
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vailing in the early 1990s, and the study was conducted
whether expressed as a proportion of MRSA among clini-
cal isolates of S aureus or the incidence of MRSA. The
decline was steady and sharp in ICUs (−59%), where control
measures have been readily implemented, and to a lesser
extent in surgical wards (−44%) that are strongly con-
connect with ICUs (many ICU patients are admitted for post-
surgical complications and return to surgical wards when
improving). In medical wards, where patients with MRSA
infections or colonizations were scattered over a large num-
er of units, likely hindering measure application, the de-
crease was less marked (−32%) and was delayed until the
launch of the ABHR campaign in 2001. During the early
years of the study, there was a trend to sharper decline in
a subset of ACHs that led the initiative and generally ap-
plied more readily the program (results not shown). In
RLTCHs, the decrease was delayed until 2001 and only
counterbalanced the increase that initially occurred in 1993
to 2001, likely due to the difficulty to implement complex
bundle measures and to hidden MRSA reservoirs in such
setting. The decrease of MRSA in blood cultures (−47%)
or pus and serous fluids (−55%) added clinical relevance
to the results, based on all clinical specimens and not tar-
ging specific infections.

The change in MRSA resistance patterns (increased
susceptibility to gentamicin), already reported in
France,22 was related to the rapid spread of new hosp-
cal clones with higher fitness that derived from older
genamicin-resistant clones,23,24 whereas clones produc-
ing the Panton-Valentine leukocidin (“community-acq-
quired MRSA”), first identified in the early 2000s in
French hospitals,25 represented less than 2% of our
MRSA cases during the survey.26 Thus, virtually all our
MRSA cases were hospital acquired, either locally or
imported from other hospitals through previous stays or
transfers, often within AP-HP, and were all recorded
to assess the global MRSA burden in our institution.
Vancomycin intermediate-resistant S aureus strains
remained scarce as reported.27
The major limitation of our study is its observational
design and lack of a control group. Indeed, the aim was
to curb as quickly as possible the high MRSA rates pre-
vailing in the early 1990s, and the study was conducted
designed as a pragmatic intervention program in our whole insti-
tution. Consequently, we should be cautious in conclud-
ing that the statistically significant association between the
MRSA decline and our control program implies a causal
association. However, several facts support such an asso-
ciation. First, previous reports from French hospitals, in-
cluding those of AP-HP, showed that the proportion of
MRSA among S aureus strains increased steadily from ap-
proximately 15% in the 1970s to approximately 35% in
the early 1990s,6-14,22 indicating that MRSA burden was not
decreasing when our program was initiated. In fact, our
program was launched in reaction to increasing MRSA rates.
These reports actually provide “preintervention” mea-
surements, which allow the present study to be consid-
ered as a “pre-post intervention” study.28,29 Unfortunately,
the number of points of measurements (1 per year)
was too low to allow a time series analysis.30 Second, the
survey was carried out at the same time each year, avoid-
ing seasonal differences, and used continuously the same
definitions. The structure and recruitment of AP-HP hos-
pitals did not change much either. Third, the efforts made
to detect MRSA did not decline over time, since (1) vol-
umes of clinical specimens did not decrease, allowing an
overall inclusion of approximately 32,000 strains of S au-
reus, and (2) national guidelines published in 2000 intro-
duced new sensitive tests to detect oxacillin resistance.16
Regression to the mean or local maturation effect are
unlikely to explain the clear and sustained decline in MRSA

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recommendations include such measures.5-7,34,36,37 The efficacy of single measures is difficult to evaluate separately,7,31,34-36,41 particularly in our study owing to its design. However, it is noteworthy that MRSA rates declined first in ICUs where active surveillance (screening) has been already shown to improve patient contact isolation at AP-HP.42-44 Screening is widely recommended34-37 and allows early contact isolation and reduction in MRSA bacteremia in ICUs.45 We did not include screening results in MRSA rates because the variability in number of beds targeted would have introduced bias.46 Importantly, MRSA rates began to decline in medical wards and RLTCHs only during period 2 of the study, ie, after launching our ABHR campaign. Extensive use of ABHR solutions is known to increase hand hygiene compliance and MRSA control36,47,48 and ABHR use is now used as a crude marker of hand hygiene in France.49 Audits on hand hygiene organized at the local institution. Partial control of MRSA was achieved in Belgian hospitals in the mid-1990s38 but was not maintained over time.3 Incidence of MRSA central-line–associated bacteremia decreased in US ICUs between 1997 and 2007, likely due to bacteremia prevention, whereas the proportion of MRSA in S aureus strains actually increased.30

Modeling studies showed that only bundled measures confer efficacy in controlling MRSA,40 and all recommendations include such measures.5,7,34,36,37 The efficacy of single measures is difficult to evaluate separately,7,31,34-36,41 particularly in our study owing to its design. However, it is noteworthy that MRSA rates declined first in ICUs where active surveillance (screening) has been already shown to improve patient contact isolation at AP-HP.42-44 Screening is widely recommended34-37 and allows early contact isolation and reduction in MRSA bacteremia in ICUs.45 We did not include screening results in MRSA rates because the variability in number of beds targeted would have introduced bias.46 Importantly, MRSA rates began to decline in medical wards and RLTCHs only during period 2 of the study, ie, after launching our ABHR campaign. Extensive use of ABHR solutions is known to increase hand hygiene compliance and MRSA control36,47,48 and ABHR use is now used as a crude marker of hand hygiene in France.49 Audits on hand hygiene organized at the local institution. Partial control of MRSA was achieved in Belgian hospitals in the mid-1990s38 but was not maintained over time.3 Incidence of MRSA central-line–associated bacteremia decreased in US ICUs between 1997 and 2007, likely due to bacteremia prevention, whereas the proportion of MRSA in S aureus strains actually increased.30

Although the decline in MRSA burden at AP-HP is very encouraging and led to generalize our initiative at the national level,35,49 the rates remained high in 2007 compared with those in northern Europe. Patients with MRSA infections or colonizations discharged from AP-HP still represent a source of secondary cases in household contacts.32 We should therefore maintain our efforts, particularly through antibiotic policy that is at present part of French national programs.49 Specific actions targeting serious infections such as catheter-related bacteremia would also contribute to hasten MRSA control.30

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Author Contributions: Dr Jarlier had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Jarlier, Marty, Andremont, Carlet, Gotti, Gottot, Nicolas-Chanoine, and Aggoune. Acquisition of data: Jarlier, Tryster, Fourrier, Carbonne, Marty, Andremont, Arlet, Buu-Hoi, Decré, Gutmann, Joly-Guillou, Legrand, Nicolas-Chanoine, Soussy, Wolf, and Brucker. Analysis and interpretation of data: Jarlier, Tryster, Brun-Buisson, Carbonne, Marty, Lucet, Brucker, and Régnier. Drafting of the manuscript: Jarlier, Fourrier, and Gutmann. Critical revision of the manuscript for important intellectual content: Jarlier, Tryster, Brun-Buisson, Carbonne, Marty, Andremont, Arlet, Buu-Hoi, Carlet, Decré, Gotti, Joly-Guillou, Legrand, Nicolas-Chanoine, Soussy, Wolf, Lucet, Aggoune, Brucker, and...

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Additional Information: Dr Jarlier coordinated the survey and wrote the manuscript. Drs Trystram, Carbonne, and Marty were the successive data managers of the survey. Dr Brun-Buisson participated in the program design and headed the AP-HP infection control committee between 2000 and 2007. Drs Fournier, Lucket, and Brücker and Ms Aggoune were successively members of the infection control team at AP-HP central administration. Drs Andremont, Arlet, Buu-Hoi, Carlet, Decré, Gottot, Gutmann, Joly-Guillou, Legrand, Nicolas-Chanoine, Soussy, and Wolf participated in the program design. Drs Andremont, Gutmann, Nicolas-Chanoine, and Soussy participated in launching the bacteriological survey. Dr Régnier initiated the program and headed the AP-HP infection control committee between 1993 and 2000.

Additional Contributions: Stéphanie Depeigne, PharmD (central AP-HP pharmacy), provided data on alcohol-based hand-rub solutions and antibiotic use; Michelle Huang (intensive care nurse, AP-HP Central Infection Control Team) analyzed AP-HP hospital reports to the central AP-HP pharmacy, provided data on alcohol-resistant Staphylococcus aureus in nosocomial spread. J Clin Microbiol. 1998;36(1):81-85.


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