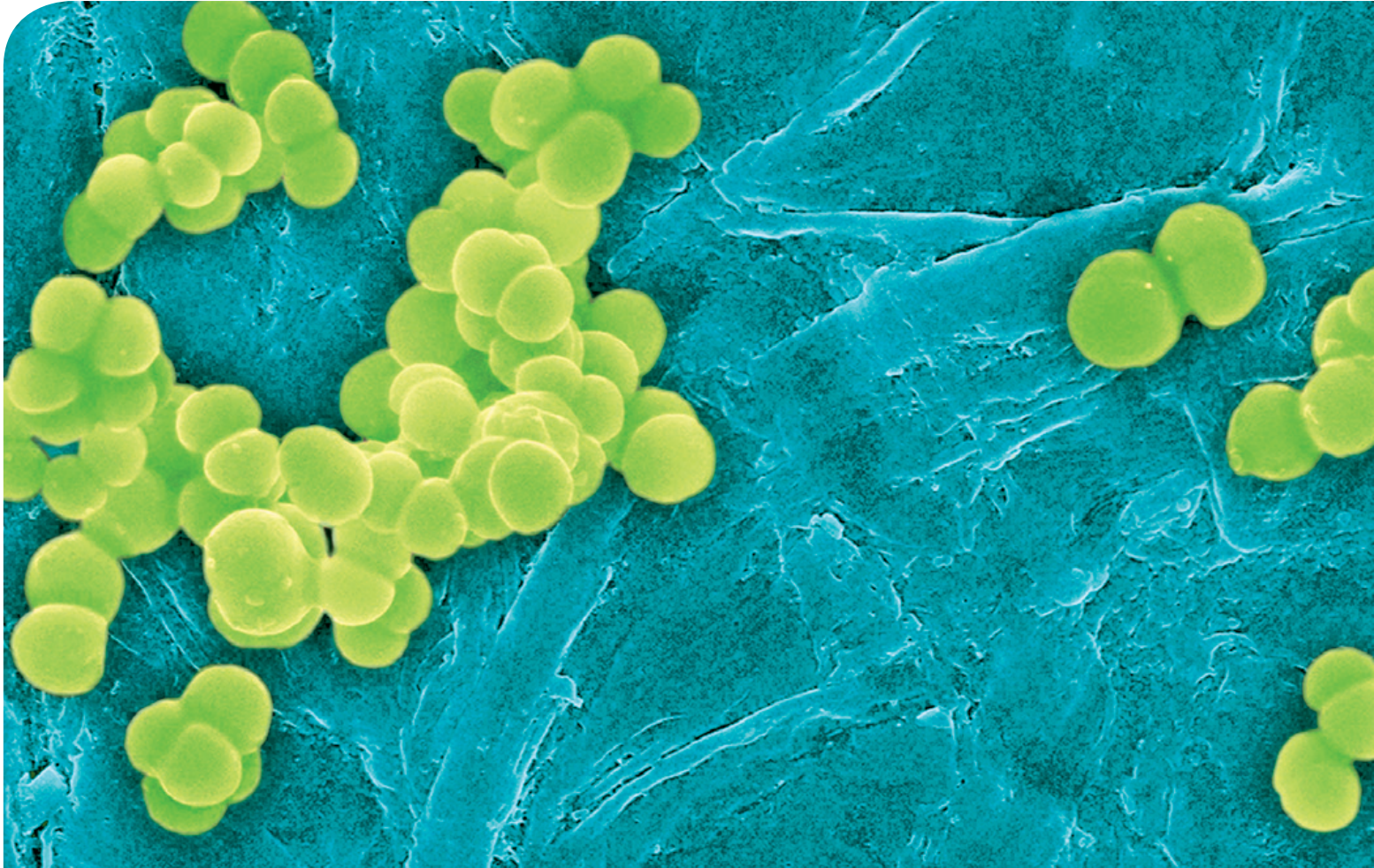schülke ✛

MRSA – a pathogen is spreading.

An updated international study overview of practiced measures to control infections.

the plus of pure performance

Contents

Preface

Staphylococci are still one of the most frequent causes of infections contracted in a hospital or in outpatient care and, among them, methicillin-resistant Staphylococcus aureus strains (MRSA) are responsible for most skin and soft-tissue infections in many parts of the world.

This topic continues to represent big challenges for responsible persons in the field of hospital hygiene with great challenges, not least because of the fact that the public is better and earlier informed through increased media reporting and more often goes to court because of the consequences of MRSA infections.

And not least because of this development, politicians address the MRSA problem as well. Measures of isolation and hygiene related to an infection caused by resistant pathogens are codable in the DRG system. Moreover, since 2009, a statutory duty of notification has been put in place regarding MRSA-positive findings in blood and liquor.

It is true that we are still not as advanced as other EU countries where even MRSA-associated deaths must be notified and where public hospitals must disclose their MRSA numbers at any time upon request. However, the start has been made in order to coordinate the standards on dealing with MRSA patients in Germany and to achieve, above all, a better interaction of outpatient and inpatient care when managing MRSA patients.

Although the general conditions are gradually improving, there is still much need for discussion and research in the field of MRSA. Many individual factors, such as the optimal approach during the 'admission screening' for MRSA, length and type of performance of an MRSA decontamination, special approaches when dealing with MRSA in neonatology and intensive care units and the question of medical staff screening still urgently require further studies in order to establish the necessary standards and to implement them. Not least because, regarding the MRSA eradication, particularly the Dutch 'Seek and Destroy' approach (including strict screening and eradication) shows how further spreading of MRSA can be contained.

The present brochure contains a collection of international study results from the past years, summarised and commented by Mr Panknin in an outstanding manner, and makes a valuable contribution to the MRSA discussion in the synopsis.

The studies show how concerned countries deal with the topic of MRSA and what can be achieved by means of consequent hygiene management.

In this context, the highly effective and well-tolerated decontamination products containing the active ingredient octenidine-dihydrochloride play an important role and could take over a key role in the future against the background of other antimicrobial substances (e.g. triclosan) whose development of resistance continues to increase strongly.

Of course, consequent hand hygiene is as important, particularly with regard to its implementation in the daily routine on the wards. Some good studies have meanwhile revealed a direct correlation between the use of hand disinfectants and the MRSA rate at hospitals.

Thanks to the thorough research of Mr Panknin, the present material can provide a good cross-sectional snapshot of the topic of MRSA. However, we must be prepared to the fact that the continuously increasing expertise on the topic of MRSA will reveal further weak points within our daily routine and therefore requires the attending medical staff to expand its knowledge in regular further education and trainings on hygiene and to implement it in practice.

Norderstedt, Germany, March 5, 2010
Boris Baur, MD | schülke I Development Antisepsis

Background

Methicillin-resistant *Staphylococcus aureus* strains (MRSA) have drastically increased worldwide over the past decade. In the US today, 40 % on average of all isolated *S. aureus* strains in hospitals are methicillin-resistant, on intensive care units even 52 %.

Unfortunately, current epidemiologic data from Germany are also showing a clear upward trend of the isolation rate over the past years. In Germany, the share of these pathogens increased between 1990 and 2001 from 1.7 to 20.7 % (data from the Paul-Ehrlich Society; *www.p-e-g.de*) (Fig. 1).
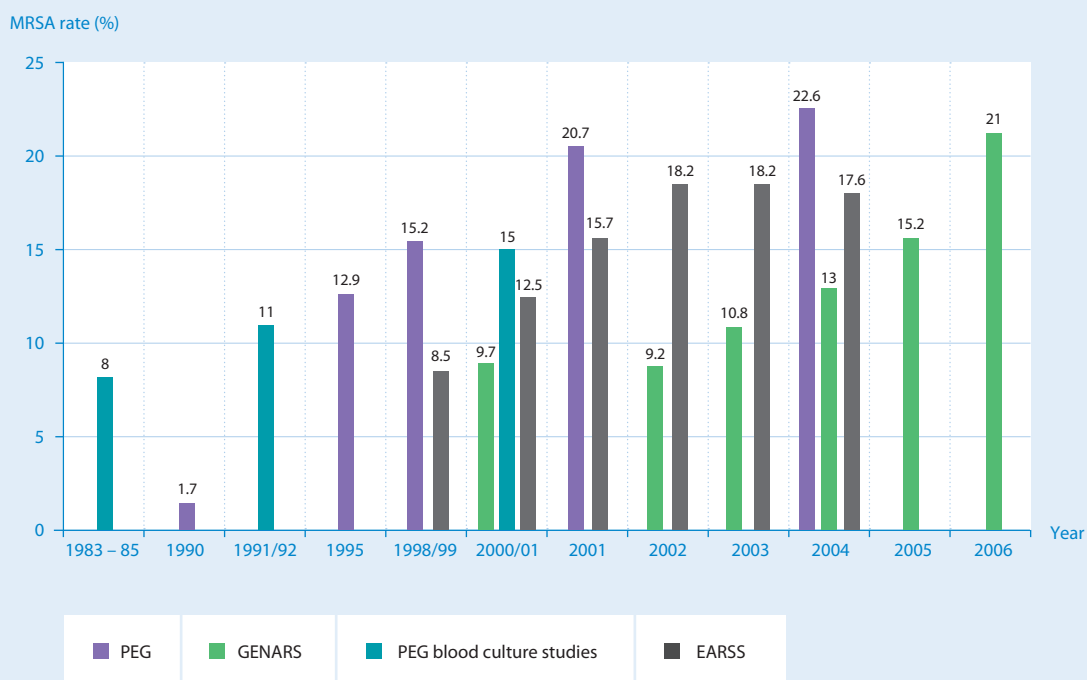

Fig. 1: Increase of MRSA in Germany. The figure includes data provided by the following professional associations:
PEG Paul-Ehrlich Society; **GENARS** German Network of Antibiotic Resistance; **EARSS** European Antimicrobial Resistance Surveillance System

1. MRSA rates compared to other European countries

However, there is still a fierce debate on the risk arising from MRSA to clinic patients.

The pathogens do not have any additional virulence factors compared with antibiotic-sensitive *S. aureus* strains (MSSA), but confront the medical staff with problems due to the mostly limited selection of still effective antibiotics. This overview presents selected, current international literature with different strategies for action in terms of prevention. However, these strategies are put into practice in very different ways!

For more than 10 years, significant differences in the frequency of isolation of methicillin-resistant *Staphylococcus-aureus* strains (MRSA) have been known between the Northern and Southern European countries.

It was repeatedly assumed that one of the main reasons for this could refer to antibiotics being too widely and too uncritically used in Southern Europe. However, at the same time, considerable differences in quality of the hospital care in terms of hygiene are known for the different EU countries.

With Dr MacKenzie, medical microbiologist at the University Hospital of Aberdeen, Scotland [3], as the head of the project, a survey was conducted in 2001 in hospitals across the European Union. The project was supported by the EU Commission and used the list of members of the ESCMID (European Society of Clinical Microbiology and Infectious Diseases).

By means of a questionnaire, the following parameters were collected from each contacted hospital:

1. Number of all isolated *S. aureus* strains in 2001 (patient-adjusted)
2. Of these strains, number of MRSA strains (patient-adjusted)
3. Use of antibiotics in defined daily doses (DDDs)
4. Resources of the individual clinics regarding hygiene staff as well as hospital hygiene activities and standards. Specifications on the last-mentioned complex of themes were collected in detail by means of 48 key questions.

24 clinics from Northern Europe, 62 from Western Europe, including Germany, 49 from Central and Eastern Europe, including the Baltic States, 55 from Southern Europe (all European Mediterranean countries as well as Israel) as well as 14 from South-East Europe (clinics from Albania, Bosnia, Croatia, Macedonia and former Yugoslavia) completed the questionnaire. With median rates of 28 % or 40 %, the MRSA rate in the South-East European and Southern European countries was several times higher than in Central and Eastern Europe, with a rate of 12 %.

The Western European countries had a median of 24 %, the Nordic countries of 0 – 1 %. A correlation with the uses of antibiotics measured in defined daily doses (DDD) per 100 bed days could be established.

A statistical calculation showed that an increase in the used amount of antibiotics by 1 DDD went along with an increase in the MRSA rate of 1.6 %. A significant correlation could be confirmed for the relation between all used groups of antibiotics, except for amino glycosides and the MRSA rate. In this context, it was interesting that the use of fluoroquinolones did not stand out as a very strong resistance trigger. However, if demographic and disease-related influence factors were also considered within the scope of a multivariate analysis (Table 1), it was shown that only the use of macrolide correlated with the MRSA rate ($r = 0.67$; $p < 0.001$) independent of these variables.

Table 1: Correlation of uses of antibiotics with the MRSA rate:
Data from 128 European hospitals

Substance group	Spearman correlation coefficient	p-value
All antibiotics	0.262	0.003
All antibiotics except for glycopeptides	0.258	0.003
Cephalosporins	0.197	0.023
Cephalosporins of the third generation	0.387	< 0.001
Fluorquinolones	0.206	0.02
Macrolides	0.200	0.02
Amino glycosides	0.149	0.09

146 hospitals provided details on the hygiene team and its activities. Among the collected variables, the following correlated in a univariate relation with the MRSA rate:

- An automatic warning system notifying the department of hospital hygiene of positive MRSA findings.
- Screening smear tests of medical staff for MRSA.
- Screening smear tests of patients for MRSA.
- Isolation of MRSA patients in single rooms (exception: patients with colonisation of the nose only).
- Use of hand disinfectants based on alcohols.

The different MRSA rate for the last-mentioned parameter was especially impressing: Clinics where no alcoholic hand disinfectants were used had an average MRSA rate of 23.7 %, i.e. almost 10 % higher than in clinics with alcoholic hand disinfection (14.2 %). In a second multivariate, statistical model, the number of hygiene professionals per 1,000 beds also correlated with the MRSA rate. The differences in the MRSA rate known from other studies in European clinics were confirmed by this study. A new finding was obtained according to which not only the use of fluoroquinolones but also the use of antibiotics in general and, above all, the use of macrolides, correlated with the MRSA rates. Alcoholic hand disinfection obviously played an important role to prevent MRSA transmissions.

A very interesting result of the study was the very low MRSA rate in the Central and Eastern European countries. This can possibly be explained by less tourist traffic in the 1990s into these countries as well as by a lower rate of patients being transferred across borders in West-East direction. It is also conceivable that generally fewer (or more conventional) antibiotics were prescribed in these countries. A disadvantage of the study is that the data have indeed been recently published, but, in the end, already date back to 11 years ago.
Whoever wishes to be up to date can visit <*www.earss.rivm.nl*> to obtain MRSA data from all over Europe.

2. MRSA infections in children: Current trend in the US

Typically, previously ill and already frequently hospitalised as well as older patients are at a greater risk of MRSA colonisation. In contrast, children are not among the typical risk groups for MRSA colonisation or infection. However, due to the increasing spreading of MRSA (community-associated MRSA, cMRSA) which have been contracted in outpatient care, this picture has changed. Particularly in the US, increasing spreading of MRSA in the age group of persons < 18 years of age has been observed. The cause is referred to cMRSA being particularly associated with suppurating skin infections and spreading via close body contact, above all in so-called 'contact sports'. They include soccer, handball, volleyball, rugby (American football) as well as wrestling and boxing. Young people practise these kinds of sports more often than older people and can suffer from skin abrasions and skin injuries. The latter offer the MRSA pathogens a point of entry.

In order to determine the current frequency of MRSA infections in children in the US, a working group around Dr Jeffrey Gerber of the Children's Hospital of Philadelphia, US [16], has recently performed a retrospective multicentre study. The study referred to a period of study from January 1, 2002 until December 31,

2007 (6 years). The data was collected by means of the Health Information System for Children's Hospitals which approx. 70 % of all big US Children's Hospitals enter their data into. The authors screened the database first of all by using the key word "MRSA" and afterwards compiled the findings of the affected patients from clinical, radiological and laboratory tests. All patients < 18 years of age were included in the study, without applying exclusion criteria.

The result showed that, in the analysed period of time, MRSA infections had been observed in inpatient patients in 33 of approx. 40 independent hospitals combined in the database system. Altogether 29,309 patients were affected. The total number of the determined *S.-aureus* infections was approx. 57,794. Thus, MRSA infections accounted for a share of 51 % of all *S.-aureus* infections. Table 2 shows the clinical parameters of the patients compared with the patients with infections caused by sensitive *S.-aureus* strains (MSSA). MRSA-infected children were on average 7 months younger and suffered significantly more often from skin and soft-tissue infections (47 vs. 33 %, relative risk 1.75). The incidence of MRSA infections clearly increased over the course of the study period (Fig. 2).
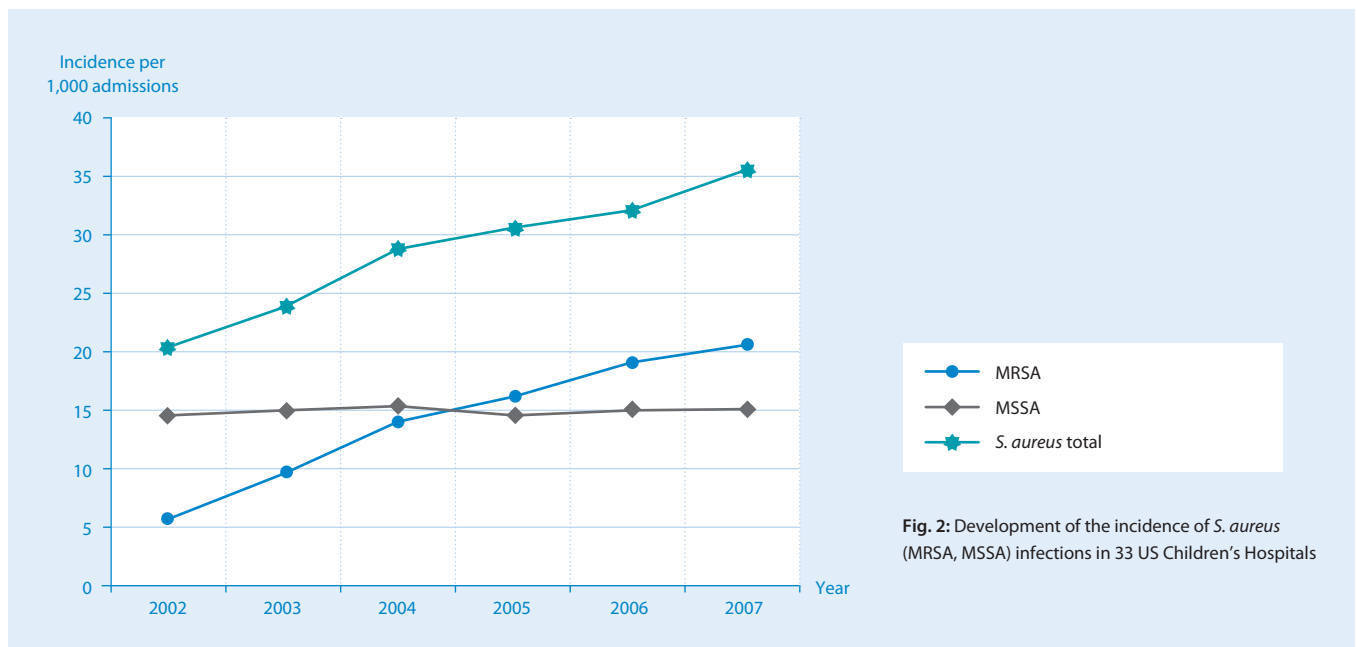

Fig. 2: Development of the incidence of *S. aureus* (MRSA, MSSA) infections in 33 US Children's Hospitals

The mortality rate of MRSA infections was 1 % and thus lower than the rate of MSSA infections.

Table 2: Characteristics of the patients

Variable	MRSA infections (n = 29,309)	MSSA infections (n = 28,485)
age, years (mean 50 % quantile)	2.8 (0.9 – 11.0)	3.5 (0.8 – 11.3)
female (%)	13,777 (47)	12,714 (45)
abscess or phlegmons (%)	13,740 (47)	9,540 (33)
osteomyelitis (%)	1,757 (6)	2,185 (8)
bacteraemia (%)	1,514 (5)	2,361 (8)
pneumonia (%)	2,856 (10)	3,135 (11)
chronic basic diseases (%)	7,559 (26)	9,814 (34)
of these, cardiovascular basic diseases (%)	2,182 (7)	3,008 (11)
discharged (%)	26,867 (92)	25,000 (88)
died in hospital (%)	360 (1)	683 (2)

The authors admit that the retrospective analysis did not enable any differentiation of the cases of infection in cMRSA cases and classical, hospital-related MRSA. However, they assume that the increase in cases in children's hospitals was mainly caused by the strongly increasing CMRSA epidemic in the outpatient sector in the US. This was particularly supported by the fact that the incidence of skin and soft-tissue infections (abscess, phlegmons) as well as osteomyelitis and septicaemia caused by MRSA increased by a factor of 5 over the study period. These types of infections are typically associated with cMRSA strains. The relatively low mortality compared with MSSA infections was remarkable.

The results underline the dramatic significance of MRSA infections in US hospitals.

The low mortality rate of MRSA-associated infections of only 1 % among the children described here underlines that the majority of them were patients without complicated basic diseases. Moreover, most cMRSA strains are sensitive against numerous staphylococci antibiotics of second choice and can therefore generally be well treated with clindamycin, co-trimoxazole and/ or rifampicin.

With abscess-forming skin and soft-tissue infections, surgical therapy also plays an essential role for a fast healing.

3. Strict policy of MRSA eradication in the Netherlands

It is well known that some, mainly Northern European countries, can exhibit constant low rates of infection with methicillin-resistant *Staphylococcus-aureus* strains (MRSA), contrary to the general worldwide trend (Fig. 3).
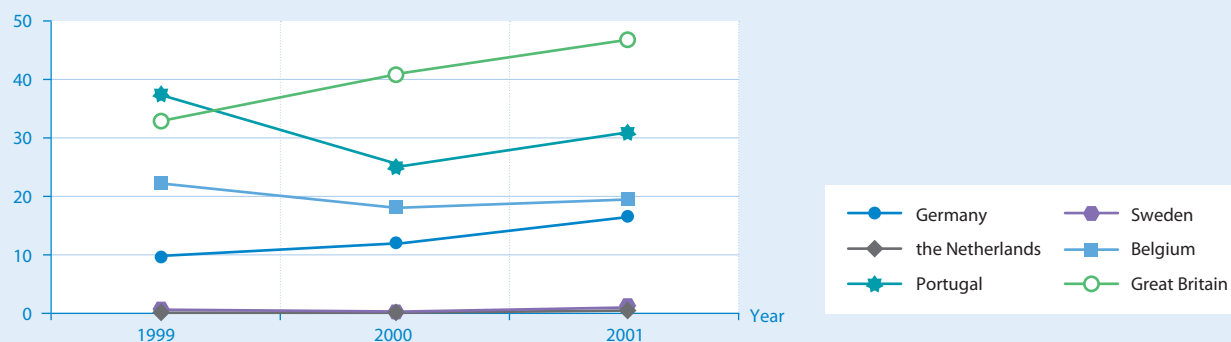

Fig. 3: Percentage of MRSA-positive blood cultures regarding all *S. aureus*-positive blood cultures in all selected EU countries.
In England, the rates increase massively due to the lack of a national MRSA policy, while the rates are low in the Scandinavian countries and the Netherlands.
Source: EARS (European Antimicrobial Resistance Surveillance, Brussels, Belgium)

These countries, such as Sweden, Norway, Finland, Denmark and the Netherlands, achieve this goal by means of a so-called 'Search and destroy' policy. This means that MRSA-positive patients are specifically searched for by means of smear tests and that these patients are kept in quarantine isolation until they are deconta-minated.

In the Netherlands, for example, all newly admitted patients and those who have already received inpatient treatment in the same or another Dutch hospital, or those who have been transferred from a hospital abroad into the Netherlands, undergo a smear test. This approach naturally involves increased costs compared with hospitals in Germany, for example, where findings of MRSA are often detected by chance during a smear test for other patho-gens.

Vriens et al. [14] from the Department of General Surgery at the University Hospital of Utrecht, Netherlands, examined the results of the expensive Dutch MRSA policy and the costs involved over a period of 10 years (1991 – 2000). The study did not only cover the Department of Surgery but the entire University Hospital of Utrecht (1,042 beds).

In detail, the following costs associated with the identification and treatment of MRSA-positive patients were determined:

- costs for microbiological smear tests
- additional material costs (for gloves, face masks, gowns)
- costs for additional medication, calculated by the pharmacy
- additional costs for cleaning and disinfection
- drop in revenue due to blocking individual beds or entire wards (in case of MRSA outbreaks)
- extra costs through release from duty of staff members colonised with MRSA and provision of substitution staff
- costs caused by sanitation of MRSA-positive staff members

Over the period of study, 1,434 patients who were previously treated in Dutch hospitals and 1,145 patients from hospitals abroad were included. 16 and 38 respectively were MRSA-positive. Apart from these specifically identified patients, only 6 further patients were determined as primarily MRSA-positive as a result of routine smear tests in the entire University Hospital during the period of 10 years – an extremely low number compared with German conditions.

Two times during the period of study, patients who at first had not been identified as MRSA-positive caused outbreaks of secondary MRSA colonisations and infections which could be controlled by means of massive measures of hygiene. Within the scope of these outbreaks, 77,800 additional smear tests were performed of which 347 (of 22 patients and 14 medical staff members) were positive.

Due to these results, corresponding costs incurred for release from duty and sanitation of the affected staff members. Table 3 compiles the costs for the MRSA policy of the University Hospital in Utrecht, Netherlands.

Table 3: Costs for the 'search and destroy' policy against MRSA in the Netherlands

Additional expenses	Explanation	Costs (€)
Cleaning	on intensive care units and peripheral wards, including 17 complete ward cleanings	207,000
Medical staff	temporary release from duty, further monitoring)	149,000
Microbiological diagnostics in patients	smear tests of patients for MRSA	673,000
Microbiological diagnostics in staff	smear tests of medical staff	280,000
Medication	additional special medication, such as vancomycin	72,000
Consumables	smear swabs, face masks, disposable gowns, etc.	213,000
Lost bed days	–	931,000
Missed surgeries	–	249,000
Overall costs	**over a period of 10 years**	**2,774,000**

At this point, the authors were confronted with the question whether such high costs are in proportion to the achieved benefit, i.e. the prevention of secondary MRSA cases.
For this purpose, the authors performed another analysis in order to calculate how many secondary cases would probably have occurred without the 'search had destroy' policy and which costs these cases would have caused.
If no microbiological screening and no preventive measures are performed, the costs listed in the table can be completely saved, i.e. the cost-saving would amount to approx. € 280,000 per year. However, according to an exploratory calculation of the authors, this cost-saving would be counterbalanced by additional expenses for antibiotics (especially glycopeptides) to treat invasive MRSA infections to the amount of € 800,000 per year.

Without any effective MRSA control, net additional costs of € 520,000 per year would be incurred to the hospital.
Even without the economic net profit, freedom of MRSA is to be strived for already for ethical and medico-legal reasons as, on the one hand, infections caused by MRSA are a heavy burden to the affected patients and can lead to long-term therapy measures and, on the other hand, they have increasingly become the subject of actions for damages.
In the Netherlands, this policy is successful as to result in current MRSA rates below 0.5 %, a value which strongly contrasts with the current German standard value of 20.7 %.

4. MRSA and mortality

Dr Sara Cosgrove et al. [1] from the Department for Infections of the Beth Israel Deaconess Medical Center at Harvard University in Boston, US, analysed all studies from 1980 to 2000 which dealt with the mortality of bacteraemias caused by *S. aureus*, and compiled the results by means of a comparative evaluation.

The question was whether bacteraemias caused by MRSA have a higher mortality than bacteraemias caused by MSSA. Altogether, the authors identified 31 studies in which 3,963 patient courses were described. 2,603 (65.7 %) of these patients suffered from a bacteraemia caused by antibiotic-sensitive *S. aureus* strains (MSSA) while 1,340 patients (34.3 %) came down with an MRSA Infection.

In 24 studies (77.4 %), mortality of infections caused by MRSA and MSSA did not differ significantly, while 7 studies (22.6 %) reported an increased mortality with MRSA bacteraemias.

However, the differences in the last-mentioned studies were pronounced to such an extent that, even if the results of all 31 studies were combined, a significantly higher overall mortality of MRSA infections remained noticeable.

The average risk to die of an MRSA bacteraemia was increased by the factor 1.93 compared with the corresponding risk of infections caused by MSSA.

A subanalysis established that outbreak situations do not have any impact on the mortality of MRSA infections: Mortality within the scope of outbreaks was almost identical to the mortality rate of all MRSA bacteraemias which occurred beyond outbreaks.

Further analyses showed that subgroups within the MRSA bacteraemias also tended towards an increased mortality rate compared with MSSA bacteraemias: The mortality rate among patients with endocarditis caused by MRSA, for example, was increased by the factor 1.79 compared with patients with MSSA bacteraemia.

The authors explain the higher mortality rate by the fact that MRSA infections are difficult to treat. It is known and has been clinically confirmed, above all in studies on endocarditis, that vancomycin kills staphylococci much more slowly than β-lactam antibiotics and that this also correlates with a delayed clinical response. In addition, the antibiogram is usually available only a few days after the drawing of the blood culture, so that MRSA infections are at first often (ineffectively) treated with a β-lactam before changing to vancomycin or recently to linezolid.

However, if the application of an adequate therapy is delayed, time is always lost and the infection progresses, which results in an increased mortality rate, particularly with severe bacteraemic clinical pictures.

5. Costs of MRSA infections

Until recently, no economic incentive caused German clinics to increasingly implement measures to early identify and prevent MRSA infections. The reason was that health insurance funds settled accounts with the clinics on the basis of bed days. This way, even longer and complicated courses due to MRSA infections could be treated with all costs covered. This situation changed all of a sudden with the introduction of the new accounting system according to the 'Diagnosis Related Groups' (DRGs) since 2004. MRSA infections can now cause a hospital considerable financial loss in individual cases. However, precise calculations regarding the amount of this loss have not been available so far. Thus, it has not been possible to calculate whether it is advisable to specifically search for MRSA (screening) upon admission of patients with certain risk factors and to decontaminate the patients. By means of an economic analysis performed in the Vivantes Clinic in Friedrichshain in Berlin, Germany, such data could be obtained for the first time. Wernitz et al. [2] studied 86 MRSA-positive patients which were identified between 2001 and 2003. The Clinic in Friedrichshain is a hospital with 700 beds and maximum care level with several conservative and surgical specialties.

Wernitz et al. determined for each case of MRSA infection the individually reimbursable DRGs and the limit of length of stay assigned to these DRGs.

It was shown that 29 % of the MRSA patients did not exceed the upper limit of length of stay; thus, these patients could be treated in the DRG system with all costs covered despite their MRSA problems. The situation is different for 71 % of the patients: They exceeded the upper limit of length of stay by 18.1 days on average. Due to the discrepancy between the reimbursement according to the coded DRG and the expenses of the hospital per care day, costs of € 8,044.18 per patient were incurred for these additional care days.

The classification according to individual MRSA diagnoses showed that the difference was greatest between reimbursement and effective costs of treatments for MRSA pneumonia and wound infection (Table 4). If the overall calculation considered that only 71 % of the patients exceeded the upper limit of length of stay, the average loss amounted to € 5,705.75 per MRSA case. After extrapolating these figures, a clinic that treats 100 patients with MRSA infection every year has to reckon with a loss of approx. € 570,500.

Table 4: Additional costs with individual types of MRSA infections in the DRG system: Data from the Clinic in Friedrichshain, Berlin, Germany

Type of MRSA infection	Average exceeding of the upper limit of length of stay in days	Average DRG revenue per patient (€)	Average costs per patient (€)	Difference between revenue and costs (€)
Postoperative wound infections (n = 21)	28.85	6,944.32	11,354.59	- 4,410.27
Pneumonias (n = 9)	28.55	6,792.49	29,277.25	- 22,484.76
Septicaemias (n = 15)	21.93	5,013.93	13,536.52	- 8,522.59
Urinary tract infections (n = 5)	14.00	2,894.36	4,656.82	- 1,762.46
Other types of infections (n = 11)	24.55	4,317.86	5,299.12	- 981.26

The authors introduced a targeted MRSA screening of certain risk groups at their clinic. A smear test for MRSA was performed immediately upon admission of patients with decubital ulcer, chronic wounds or diabetic gangrene. A smear test was also performed on patients from old people's homes and nursing homes, from other hospitals with known MRSA problems and patients with earlier MRSA problems.

This screening led to a clear reduction in the invasive MRSA infections in the clinic. Wernitz et al. calculated that the screening saved annual costs of treatment to the amount of **€ 110,236**. Regarding this saved amount, the relatively low costs of the screening were already deducted.

6. Change of MRSA in public awareness

In the meantime, a clear change in how to deal with this problem has become noticeable in some countries. In England, health authorities have done a complete about face after the Freedom of Information Act became effective in 2005. This law, originally formulated due to the poor transparency of government information on the War in Iraq, guarantees the public free access to internal information of public institutions, as long as they do not affect personal rights.

Since community hospitals are also subject to this regulation, MRSA rates of many English clinics have recently been available on the internet or are published in the local press. The numbers were partially alarmingly high and put pressure on the clinic managements to act and to implement hygiene programs – hygienists and hygiene professionals in England are experiencing an economic boom at the moment.

Moreover, the headlines in the daily press also put the Health Minister under great pressure; he promised the parliament to halve the MRSA rates by 2010.

Similar things are happening in the US where multicentric MRSA control programs have been started in some states. In Japan, too, people make an effort to actively control MRSA in big clinics. In Germany, the latest numbers of different networks show a trend that the epidemiologic curve is flattening out and entering a plateau phase.

This could be achieved at individual clinics by means of committed hygiene programs which were mostly implemented according to the principle of a package of measures. In contrast, in the Southern European countries, considerable indifference unfortunately still prevails regarding the implementation of effective hygiene programs to control the MRSA epidemic.

The reason for this is the funding of community hospitals which is too low for patients with statutory health insurance. Many clinics do not dispose of sufficient isolation rooms and of utensils for barrier care either, such as long-sleeved gowns with armbands or isolation vehicles.

7. How often is MRSA transmitted through contact while performing simple care tasks?

Gloves are to be worn only during care measures involving direct patient contact or during medical examinations involving direct contact with the patients. Even if this is observed, the gloves are unfortunately all too often not taken off immediately after the patient-related measures. On the contrary, display user interfaces, round vehicles, among others, are often touched or notes are entered into the curve. Unfortunately, telephones and computer keyboards are also touched all too often with already used gloves.

The risk of being contaminated with MRSA at the hands or gloves already after one single care measure with a patient has meanwhile been analysed in a prospective microbiological study. McBryde et al. from the Princess Alexandra Hospital in Brisbane, Australia [15] set up a so-called 'hand massage cultures' of the hands of the staff members.

The study was conducted over the period from July to December 2003 and was performed on MRSA patients in all hospital areas. Physicians, consultants, medical staff members and physiotherapists who entered an MRSA room were asked, upon leaving it, to immerse one hand into a sterile plastic bag filled with 50 ml of an irrigation solution. The bag was tightly closed onto the wrist and thoroughly massaged for 1 minute, so that MRSA pathogens on the hand were transferred into the irrigation solution. Afterwards, the individual staff member was asked to wash his/her hands thoroughly with a medical soap. After being washed, a sample was taken from the other hand just like the first hand by applying a "hand massage". The order of the hands (right or left hand first) was individually determined by tossing a coin.

The irrigation solutions were then examined microbiologically; however, for technical reasons, only 0.5 ml, i.e. a hundredth, could be examined from the originally obtained 50 ml irrigation solution from each hand.

Samples could be taken from 129 staff members; the hand culture of 17 (13.2 %) of them was MRSA-positive after patient contact. Regarding staff members wearing gloves, a sample was taken from the 'gloved' hand. As assumed, the MRSA contamination rate was almost the same for gloved hands and unprotected hands (contamination of persons wearing gloves 12/93 = 12.9 %; of persons without gloves 5/36 = 13.9 %).

Only 3 in 5 staff members, who had not worn any gloves, were able to remove MRSA by means of hygienic hand washing. One staff member who had worn a glove was still MRSA-positive under the glove despite washing. Unfortunately, the effect of alcoholic hand disinfection was not examined.

A small secondary result of the study should be mentioned: The question arises again and again whether disposable gloves which are available in an MRSA room in an open glove box may not be contaminated with MRSA. Therefore, McBryde et al. set up bouillon cultures of gloves from such boxes in close proximity to the MRSA patients.

MRSA contamination was not confirmed for any of the 100 examined gloves. The compliance regarding the use of gloves with direct patient contact was documented in the study as well. It was best with ward assistants and worst with physicians (Table 5).

Table 5: Use of gloves regarding measures in MRSA rooms

Type of staff	% use of gloves with direct patient contact in MRSA rooms
Nursing staff	76
Physicians	27
Physiotherapists	83
Ward assistants	91
Kitchen helps	75
Cleaning service	75

The results can be summarised as follows:

(1) The transmission rate of MRSA to the hands after performing a simple medical/care task on a patient amounted to 13.2 % on average.
(2) The transmission to the hands occurred similarly both to ungloved and gloved hands.
(3) The compliance regarding use of gloves was especially poor with physicians, and best with ward assistants.
(4) Hand washing, even if performed by using antiseptic soap, led to effective decontamination only in 3 out of 5 cases.

It is a very alarming but probably a realistic result that the hygienic requirement to wear gloves in case of direct contact with MRSA patients was not met by 36/129 (27.9 %) of the staff members in the present study. This shows further education measures and trainings probably have a considerable potential for improvement!

In such trainings, the results obtained from this study are very useful. If approx. 13 % of the medical and care contact with MRSA patients lead to contamination of the hands, using gloves – even with frequent change of gloves – should clearly be cost-effective.

A drawback of the study was the performance of hand washings for hand decontamination. Unfortunately, simple hand washing with antiseptic ('medical') soap is still the only hand hygiene measure in Anglo-Saxon countries.
The study clearly shows that only approx. 60 % of the hands can effectively be liberated from MRSA this way.

Alcoholic hand disinfection, as it has been established in Germany and other European countries for decades, would certainly result in an effective decontamination of > 99 % of the hands – provided that it is properly performed (6 steps) with a contact time of 30 seconds and complete moistening.
Fig. 5 illustrates the particularities of hygienic hand disinfection.

Particularities of hygienic hand disinfection

Using sufficient amount of disinfectant →

Applying correct rub-in method ←

Observing the contact time →

Using a disinfectant of impeccable quality ←

Fig. 5
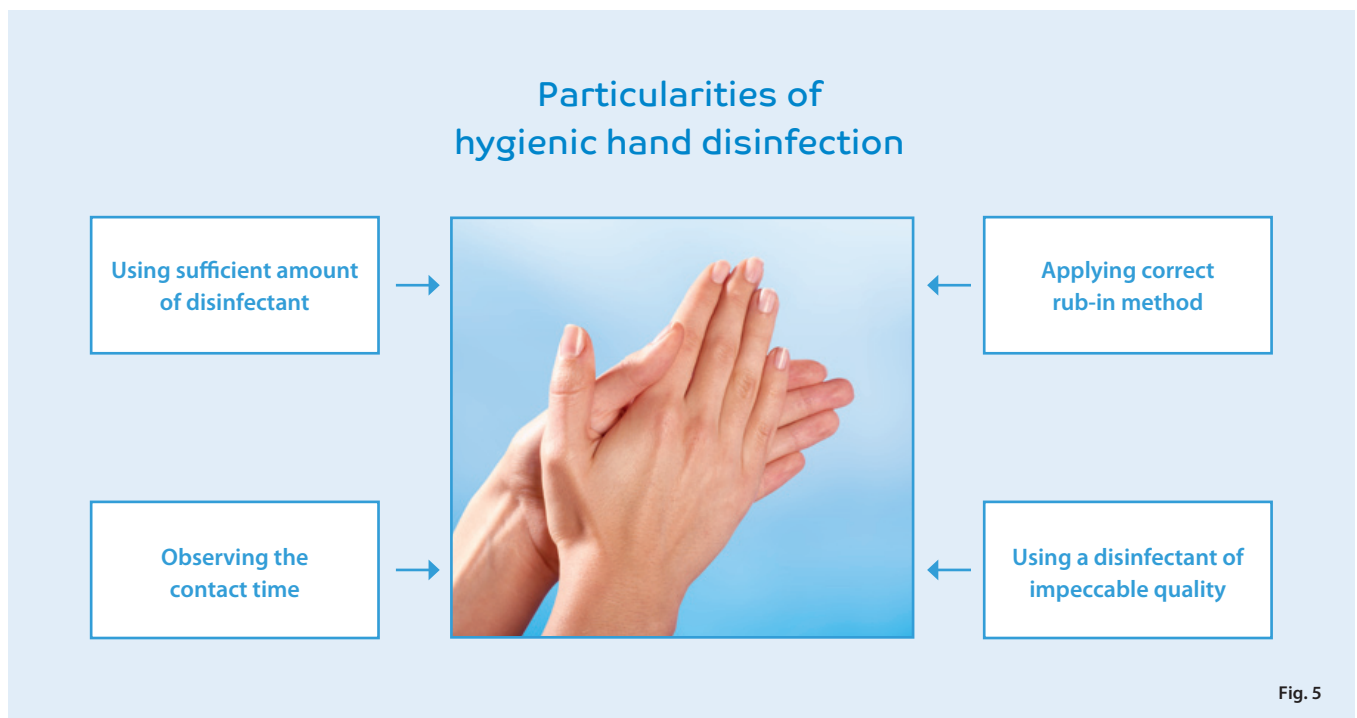
8. Prevention of infection –
standards to contain MRSA epidemic

In relatively manageable federal state, the island state Rhode Island at the East coast of the US, the attempt was made to minimise the rates of transmission of this pathogen by applying an MRSA policy aligned between all hospitals. The reason for this coordinated action was the increase of the MRSA contamination rates from 0.3 colonisations/infections per 1,000 patient treatment days in 1995 to 1.2 per 1,000 patient treatment days in 2001.

The infection specialists of the 5 big acute hospitals of Rhode Island [4] set up a task force with the aim to unify the already existing MRSA standards in the individual hospitals.

The consensus guideline prepared during several meetings within 8 months includes statements on the following questions:

- When are smear tests indicated with newly admitted patients?
- In which situations must MRSA smear tests be performed on hospital staff members?
- Which measures are to be taken for so-called contact patients, i.e. patient who were lying down next to a patient who was later identified to be an MRSA carrier?
- What are currently recommended isolation measures for MRSA patients?
- How are MRSA-positive patients to be decontaminated?
- When can the isolation be discontinued?
- What measures are to be taken in the outpatient sector?

Differentiated answers to these questions are presented and, if applicable, also include several possibilities depending on the individual situation. Table 6 provides a simple summary of the standards.

Table 6: MRSA standards in Rhode Island, US

	Measure	Type of performance, if applicable, duration or frequency
Newly admitted patients • from nursing homes • from another acute hospital • dialysis patients • readmission after ≤ 30 days	Screening smear tests	Nose smear, if necessary, wound smear test; performance within 24 – 48 h upon admission.
Hospital staff members		**No routine MRSA smear tests!** Only in case of outbreaks involving MRSA strains affecting several patients on the ward.
Contact patients		Nose smear on contact patients if the patient was laying down ≥ 24 h next to the index patient.
Isolation of MRSA patients	• single room • gloves for all persons entering the room • gowns for all persons dealing with the patient or who touch the surrounding • masks for all persons if the patient's respiratory tract is colonised (without and with ventilation)	Possible accommodation in cohorts of several MRSA patients in one room. If the patient has to leave the room (e.g. for X-ray), he/she must put on fresh clothing and a mask, as well as disinfect the hands.
Decontamination of MRSA patients	• colonisation of the nose: antimicrobial nose ointment, e.g. Mupirocin • colonisation of the body: antiseptic washing with a preparation containing chlorhexidine/hexachlorophene	Continuation over 3 to 5 days. Control smear tests 48 h after the end of the treatment at the earliest.
Regulation for visitors	Gloves, gowns and masks (the latter only if the MRSA patient's respiratory tract is colonised).	Disposing of protective clothing, masks and gloves before leaving the room.
Discontinuation of the isolation	If 2 successive smear tests are negative.	Smear test of all previously positive areas of the body. Interval between the control smear tests must be of at least 5 days.*
Measures in outpatient sectors	• call in MRSA patient at the end of the day in the outpatient department • Patient can wait in the normal waiting area	Protective measures (gowns, gloves, masks) are the same as for inpatient patients.

*   No agreement was reached on this recommendation; one part of the working group favoured discontinuing the isolation already after one negative series of smear tests.

In December 2001, the recommendations were distributed to all chief physicians of clinical departments in Rhode Island and – as far as the authors know – have been implemented in all clinics since then. No data are currently available on to what extent the MRSA incidence can be minimised this way. Regarding some of the mentioned questions, the authors still see a need for research, such as in the question whether a patient can be removed from the single room already while the decolonisation treatment is still ongoing, whether visitors really have to put on protective clothing on the entire body, or whether one or two series of smear tests are required for follow-up. The MRSA rates in Rhode Island shall continue to be indicated as contamination rate per 1,000 patient treatment days.

The previously mentioned recommendation differs only in a few aspects from the MRSA guideline published by the Robert Koch Institute in Germany (Notification of the Commission of Hospital Hygiene and Prevention of Infection at the RKI:

Recommendation on the prevention and control of methicillin-resistant *Staphylococcus aureus* strains (MRSA) in hospitals and other medical facilities.
Federal Health Gazette – Health Research – Health Protection, [1999] 42: 954–958). The RKI recommends, for example, 2 smears from the nose and pharynx as a screening measure, whereas the Americans consider one smear from the nose to be sufficient. After completion of the decontamination measures on patients, in Germany, the RKI recommends smear tests 3 days after the end of treatment at the earliest; isolation can be discontinued if two further series of smear tests on day 4 and 5 are negative.

It is interesting that the German RKI guideline describes surface disinfection in the patient room and of contact surfaces in detail whereas the Americans do not mention it at all! This shows that the role of surface disinfection is differently evaluated in the two countries.

9. Hygiene measures for MRSA-positive patients – which measures have been confirmed by scientific evidence?

The scientific data base on dealing with MRSA in terms of hygiene was the subject of a critical assessment within the scope of a comprehensive literature analysis. Dr Marshall et al. from the Epidemiologic Department at the Monash University in Melbourne, Australia [5], performed a Medline literature search without time limit using they key words 'MRSA' and 'methicillin-resistant *Staphylococcus-aureus*'. The literature list of the obtained works was combed through for further relevant publications.

The finally obtained material was divided into the following sections and separately analysed:

1. measures by means of which a selection of MRSA in a population of *Staphylococcus aureus* can be prevented,
2. measures by means of which the pool of colonised patients can be decreased,
3. measures to prevent an MRSA infection in colonised patients, and
4. measures to prevent a transmission from patient to patient.

The research of the authors on these four sets of themes obtained the following results:

Ad 1. It has been confirmed in a series of observational studies that high uses of antibiotics in hospitals correlate with increased MRSA rates. The literature analysis showed that certainly not only fluoroquinolones, but also other substances lead to a selection of MRSA. However, it has not been confirmed that limiting the use of antibiotics in general or reducing the application of certain substances conversely reduces the MRSA frequency. One of the studies showed that the rate of MRSA isolations could be reduced by means of a rotating use of antibiotics on an intensive care unit (so-called 'cycling') – however, the authors had improved hand disinfection in parallel to the changes in the antibiotic regime (Raymond DP et al., Impact of a rotating empiric antibiotic schedule on infections mortality in a ICU. CritCare (2001)29:1101 - 1109). As randomised studies on this question cannot be performed for ethical reasons, at least an interventional study (before and after comparison) would be desirable from the authors' perspective.

Ad 2. Most clinics perform a decontamination treatment with Mupirocin, mostly over a period of 5 days, after a contamination of the nose has been confirmed. In addition, antiseptic washings of the whole body are performed, e.g. with shampoos or solutions containing chlorhexidine, if MRSA has been confirmed on the skin of the body. The value of these measures has been confirmed by scientific evidence only for outbreaks, but not in an endemic situation. The only published randomised, controlled study showed only a mediocre, statistically insignificant reduction in the rate of MRSA colonisation compared with the patients treated with placebo. With nasal Mupirocin treatment, the MRSA carrier rate of the originally MRSA-positive patients decreased to 56 %, without Mupirocin treatment to 81 % (Harbarth S et al., Antimicrob Agents Chemother [1999];43:1412-1416). This minor effect was all the more outstanding as both groups were simultaneously treated with chlorhexidine washings. One study in which a single nose treatment was compared with a nose treatment in combination with body washings with chlorhexidine solution did not establish any significant difference. In both groups, the nasal carrier rate finally reached the same level again after some weeks (Watanakunakorn C et al., Am J Infect Control [1995];23:306-309). However, the study was not extensive enough regarding the number of included patients in order to answer this question with sufficient informative value.

Ad 3. Preventing an MRSA infection in a colonised patient: colonisation of the nose with *S. aureus* (not only MRSA, but also MSSA) correlated in a series of studies with subsequent invasive infections. The studied collectives included, for example, cardiac surgery patients, patients with liver cirrhosis, HIV patients or liver transplant recipients. However, it is less well proven that, inversely, an eradication of *S. aureus* from the nose reduces the risk of a subsequent invasive infection. All of these studies were performed without focusing on MRSA but on all patients or all *S.-aureus* positive patients. However, their results are probably transferable to MRSA-positive patients, as MRSA and MSSA are comparably sensitive to Mupirocin. Altogether, it can be established that the risk of postoperative sternal soft-tissue and bone infections could be reduced by means of prophylactic eradication of *S. aureus* from the nose only in cardiac surgery patients.

Ad 4. Regarding their effectiveness, the measures implemented in many clinics, such as isolation in single rooms or in cohorts, wearing gowns or gloves and using masks are unfortunately not as well proven by study data as generally assumed. Two studies performed on intensive units, however in a highly endemic MRSA situation, even show that the isolation in single rooms does not have any effect (Cepeda JA et al., Lancet 2005;365:295-304; and Nijssen S et al., Clin Infect Dis [2005];40:405-409). However, the studies were much criticised on their methods, which becomes clear by the numerous reader's letters. Neither are data available that provide evidence that a microbiological screening of staff members leads to a reduction in MRSA rates. In contrast, it has been demonstrated in many very good studies that a microbiological screening performed on admission to the hospital contributes to the reduction in secondary MRSA infections and is thus also cost effective. The screening can be limited to certain patients at risk (e.g. > 65 years of age, diabetes mellitus, chronic wounds, dialysis patient) (Papia G et al., Screening high-risk patients for MRSA on admission to the hospital: is it cost effective?) Infect Control Hosp Epidemiol (1999) 20: 473 - 477). The individual impact of today's generally employed measures of hygiene for MRSA patients has not been well evaluated scientifically. Only a series of studies is available in which an overall concept of different measures was finally successful. According to the authors, there is urgent need for studies in which (1) the question of a continuative microbiological surveillance of hospital patients for MRSA and (2) the role of single room isolation or accommodation in cohorts is scientifically precisely evaluated. Unfortunately, the authors are right in many aspects.

For example, it is not clear in which situation screening smear tests are to be performed on the staff members and when, for example, searching for MRSA on inanimate surfaces (so-called 'surface tests') is useful. Both are probably measures which only cost money but do not lead to any reduction in the MRSA rate in the endemic situation. Neither has it ever been examined whether continuative surveillance cultures, for example, once a week in patients on intensive care units, can reduce MRSA transmissions. Regarding MRSA, only the following can be mentioned as evidence-based measures:

- MRSA screening of patients at risk on admission (nose smear is sufficient)
- Nasal decontamination of *S. aureus*-positive (incl. MRSA-positive) patients using Mupirocin prior to cardiac surgeries.

The present work is only one in a series of publications dealing with the usefulness of individual measures of hygiene for MRSA. However, results obtained from other researches in this topic were similar. The reader will find a very good systematic literature analysis, for example, by Cooper BS et al., Brit Med J (electronic version) [2004];329:533, p. 1– 8.
The study is available at *www.bmj.com*.

10. Disputes about single room isolation – current state of studies

The decision regarding which measures should be best suitable to contain MRSA transmission is however not easy to make. Controversial statements by individual scientists and working groups on individual measures are again and again published.

In this context, a longitudinal study performed on 2 London intensive care units and published in 2005 by a London working group plays a very negative role [6]. In chronologically successive study phases, the authors compared a single room or cohort isolation of MRSA patients involving an approach according to which only gowns and gloves were used at the beds without spatial separation of the patients.

The result did not show any difference in the rate of MRSA acquisition, so that the authors concluded that spatial isolation was ineffective. However, the study was afterwards much criticised on its methods. The isolation areas in which MRSA-positive patients were accommodated in cohorts were partially not separate rooms, but only open bed bays. On one of the wards, a common counter was used to document care and prepare utensils and from which patients colonised with MRSA were supplied as well. Neither did the study include a general screening on admission, so that numerous MRSA patients were probably not or only later identified.

11. New studies provide evidence of the effectiveness of isolation/accommodation in cohorts

In the meantime, several studies which have been planned more carefully with regard to their methods have shown that previously increased MRSA rates can be reduced by means of consequent spatial separation of positively tested patients. As a counter-reaction to the London study, Scottish physicians at the Royal Hospital in Aberdeen (1,200 beds) performed a before and after study on their mixed intensive care unit with 16 beds.

During the lead time of 24 months, MRSA patients were only identified based on clinically indicated smear tests (e.g. tracheal aspirate in case of fever and purulent tracheal secrete) and cared at their individual beds. Starting in month 25, MRSA smear tests were performed on each newly admitted patient as a matter of routine. Patients known to be MRSA-positive or those newly

identified were isolated in single rooms or in cohorts. In each individual case, decontamination treatment with antibacterial nose cream, pharynx irrigation with antiseptics and daily body washings was performed until transferral or discharge from the intensive care unit. The result of this study showed that the MRSA incidence could be reduced by 60 % after introducing this program. Of the patients who were tested positive for MRSA, 49 were only identified through the newly introduced routine screening. The rate of MRSA-positive intensive care patients decreased from on average 16 % to 6 % (Fig. 5), the rate of MRSA bacteraemias fell from 29/1232 (2 % of the patients) to 11/1421 (0.8 % of the patients).
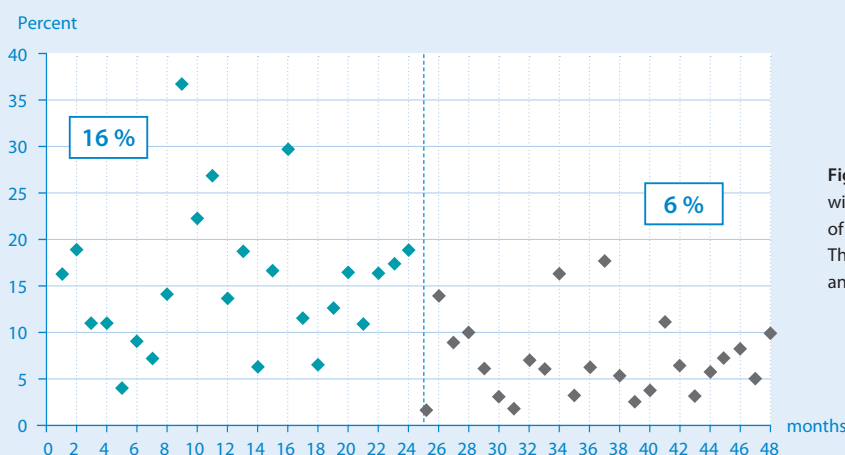
Fig. 6: Percentage of the intensive care patients with confirmed MRSA before and after introduction of general screening.
The boxes indicate the average value of the before and after period. According to Gould et. al. [7]

The specificity of the achieved effects could be provided evidence of by the fact that the frequency of methicillin-sensitive *S.-aureus* strains, gram-negative enterobacteriaceae with formation of extended-spectrum β-lactamase (ESBL) as well as of resistant Pseudomonas and Acinetobacter strains remained unchanged [7]. Corresponding to the decrease in MRSA cases, the use of vancomycin decreased as well from 35 DDDs/100 bed days at the end of the period before to 20 DDDs/100 bed days at the end of the period after. The additional costs for screening and isolation amounted to approx. £ 11,000 (approx. € 16,000); however, they were probably completely compensated by avoiding 18 cases of MRSA bacteraemia [7]. Since this study, single room isolation can be considered an effective means to reduce MRSA transmission, as long as it is combined with screening on admission and consequent decontamination treatment.

A longitudinal study with a somewhat different design, but with a similar purpose, was performed at the Brigham and Women's Hospital in Boston, Massachusetts, US [8].
The authors documented the rate of MRSA-associated septicaemia of all adult hospital patients over a period of 9 years. Individual measures of hygiene, such as for example trainings to improve hand hygiene as well as the introduction of alcoholic hand disinfectants did not have any significant impact on the MRSA bacteraemia rate. The septicaemia rate could be reduced significantly only in 2003, after a general screening on admission had been introduced for all patients newly admitted to the intensive care unit. The incidence of secondary MRSA cases among patients at risk (MRSA confirmed > 2 days after admission) decreased from 43 secondary MRSA cases/1,000 patients at risk in the first half of the screening period to 23 cases/1,000 patients at risk in the

second half ($p < 0.001$). The incidence density of MRSA cases decreased by 67 % on the intensive care units and by 39 % on the peripheral wards; in the entire hospital, a total decrease by 53 % could be achieved. The impact on the MRSA screening on peripheral wards could be explained by the fact that MRSA patients could be transferred to the periphery already with a corresponding 'advance warning' and that altogether fewer MRSA cases occurred on the intensive care unit. The prerequisite for this success was consequent single room or cohort isolation of all patients identified as MRSA-positive. However, it was interesting that this study did not include any decontamination treatment – the success was purely achieved by means of spatial isolation and 'barrier care'.

Conversely, a recently performed study at a Japanese hospital with 1,100 beds showed that even an intensified hygiene program does not lead to any success worth mentioning without the possibility of spatial isolation [9]. The MRSA rate increased from 58.4 to 61.4 % despite additional staff members to the hygiene team, employment of a statistician to document and to provide feedback on the surveillance results and a hand hygiene campaign with posters.
The dramatically high numbers (60 of 100 isolated *S.-aureus* strains were MRSA!) demonstrate that the epidemic in Japan got out of control. Single room isolation is no longer possible there, as no hospital can provide the majority of the patient with single rooms. Even accommodating these patients in cohorts would practically paralyse the hospital operation. This shows that countries whose MRSA rate is still below this level are well advised to bend the MRSA curve in time.

12. Decontamination treatment: useful or ineffective?

New clinical data enabling a quantification of the expected success rate are available also regarding the decontamination treatment.

Wendt et. al. [10] published a study which evaluated altogether 114 analysable patients from the University Hospital of Heidelberg, Germany, and from nursing homes in the surroundings, and compared the effect of a 5-days antiseptic washing of the whole body with a washing with detergents only. A solution containing 4 % chlorhexidine was used as an antiseptic washing preparation.

The oral decontamination therapy was performed with a solution containing 2 % chlorhexidine, the sanitation of the nose with Mupirocin ointment. The control group used care preparations with identical appearance as a placebo.

The result showed a significantly better effect of the antibiotics or antiseptic treatment compared with placebo only in one MRSA colonisation of the nose and the groin.

However, it should not be concluded that a decontamination treatment with active substances is no use.

The comparison with a placebo group is not necessarily relevant to the result of the treatment, but it is rather decisive how many patients could be sanitised in the end.

Of the originally 27 nasal *S.-aureus* carriers, only 6 were still positive after completion of the treatment with Mupirocin, which corresponds to a success rate of 78 %.

Other authors have achieved a sanitation success of up to 95 % of the cases among patients with nasal colonisation with *S.-aureus* [11]. Concerning nose carriers only, an eradication attempt with Mupirocin is thus definitely useful and promising. Whether an antiseptic washing of the whole body is useful has to be decided individually. Patients with chronic wounds seem to be difficult to decontaminate as the wounds serve as an MRSA reservoir and a new colonisation of the body can easily emerge from them. Here, it should be focused on effective wound therapy, as the MRSA reservoir is sanitised as well with a successful closure of the wound.

13. Antibiotic-free sanitation of MRSA-positive medical staff

A recently published work from the University Hospital in Greifswald, Germany [18], in which routine data of MRSA sanitation of staff members and relatives were retrospectively evaluated over a period of 24 months in order to verify the efficacy of the sanitation with the antiseptic active ingredient octenidine as first-line therapy, showed that 98.1 % out of 107 treated persons could be successfully sanitised.

The concept of treatment involved on the one hand a holistic decontamination with octenidine and consisted of a nose ointment (0.05 % content of active ingredient), a preparation to wash skin and hair (0.3 % content of active ingredient) and a mouthwash (0.1 % content of active ingredient).

Furthermore, hands and surfaces were decontaminated. In 73 cases (68 %), antibiotic-free sanitation was already achieved in the first cycle (Table 7). Sanitation with octenidine-based preparations proved to be effective and well-tolerated over the studied period of time. With regard to increasing resistances against Mupirocin, a randomised, controlled study should follow to verify this concept of treatment.

Table 7: Sanitation rate (percent per cycle, accumulated for the total number) with decolonisation of staff members according to the Greifswald scheme (n = 107)

Cycle	negative	Rate of sanitation (%)	Accumulated share (%)
1.	73	68.2	68.2
2.	27	79.4	93.5
3 and more	5	57.1	98.1
Lost on follow up	(2)	n. a.	1.9
Overall sanitation rate			**98.1**

The study situation on the efficacy of MRSA sanitation is heterogeneous. The results are comparable only to a limited extent, due to considerable differences in the schemes, outcomes and studied patient collectives.

14. MRSA in hospitals – successful hygiene in a German hospital of maximum care

A German hygiene study by Trautmann et al. [12] described the success of a coordinated hygiene program at the Katharinen-hospital in Stuttgart, Germany, a hospital of maximum care and with approx. 900 beds. Both colonisations and invasive infections caused by MRSA could be significantly reduced within 5 years (2002 – 2006).

After a continuous increase in MRSA cases in the 1990s, the number of cases culminated in 2002 with approx. 200 new cases; this corresponded to an incidence of 79 cases per 10,000 new admissions. In 2002, a hygiene institute was founded and defined the containment of the MRSA problem as its priority goal.

The developed, coordinated MRSA program was prepared in writing and made public by means of trainings, meetings of the hygiene commission as well as of regular feedback events on the wards.

Measures of hygiene, such as single room isolation, use of gowns/gloves and room disinfection after discharge were strictly implemented.

The program was funded with investments on behalf of the hospital's business management: Among others, 1,700 textile gowns with armbands in signal yellow for the care of MRSA patients as well as 12 MRSA trolleys were acquired. These ward trolleys were closed trolleys and all utensils ranging from gauze to blood pressure cuff required for the care of MRSA patients could be stored in them.

After discharge or successful sanitation of an MRSA patient, the trolley was disinfected externally by means of wipe disinfection and sealed and, in this form, was ready for the next admission of an MRSA patient.

15. Halving the incidence of secondary MRSA cases

As a result, a remarkable success could be achieved in the following years: The incidence of new MRSA cases decreased by 29 % from 79 to 56 per 10,000 new admissions. In a lecture held on April 20, 2008 in Berlin, Germany, Trautmann stated that the incidence in 2007 could be decreased even further (Fig. 7).
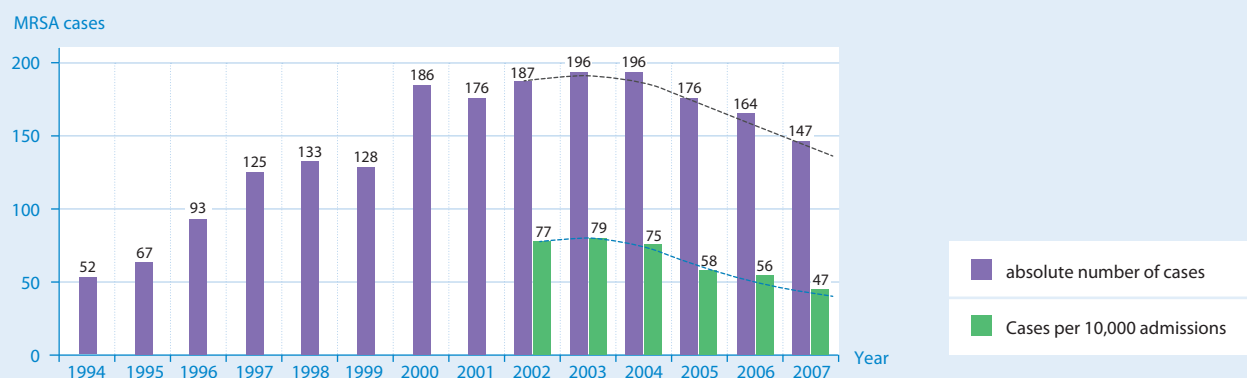
MRSA cases

Year	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
absolute number of cases	52	67	93	125	133	128	186	176	187	196	196	176	164	147
Cases per 10,000 admissions									77	79	75	58	56	47

Fig. 7: Hygiene program at a clinic of maximum care:
Decrease in the absolute number of cases and the number of cases per 10,000 admissions since 2003.

A differentiation of the cases in 'MRSA imports' from outside and internal 'MRSA transmissions' showed that, at the beginning of the program, 60 patients with already existing MRSA colonisation were admitted from outside or externally; this number increased until 2006 to 91 cases per year (52 % increase). In comparison with these unavoidable MRSA imports, the number of secondarily transmitted cases fell from a peak value of 131 (2003) to 57 (2007), i.e. a reduction by 56 %.

The transmission index calculated by the authors (secondary cases divided by imported cases) decreased from initially 2.1 to 0.6 in 2007. In addition, using the Hospital Infection Surveillance System (KISS system), the authors documented the incidence of invasive MRSA infections on the surgical and the medical intensive care unit as well as in the clinic for orthopaedics and trauma surgery. On the intensive care units, the incidence of MRSA pneumonias fell from 1.47 to 0.71, of septicaemias from 0.4 to 0 and of urinary tract infections from 1.98 to 0.71. An essential part of this decrease could be contributed to by the general screening on admission of surgical intensive care patients. Before its introduction in 2003, half of all MRSA-positive patients had obviously been 'missed'.

Although the costs of the program were not available in detail, the authors calculated that approx. 472 MRSA cases were prevented between 2003 and 2007. A study recently performed in Germany on the costs of MRSA in the DRG system concluded that one MRSA case causes on average a loss in revenue of € 6,600, even if the new reimbursement code 'complex treatment of multiresistant pathogens' is applied [2].
As a result, by preventing 472 cases, loss in revenue to the amount of approx. € 3.1 million had been prevented.
An important prerequisite for the success of the program was the fact that is was implemented across disciplines in all clinical departments and predominantly on the intensive care units.
According to Trautmann, another aspect was decisive: Different professional groups, such as medical staff, physicians, physiotherapists and radiology professionals were involved in the program from the beginning and actively participated actively.
The program was led by a four-member hygiene team, including one health scientist, two hygiene professionals and the clinic hygienist.

16. Management of MRSA outbreaks on neonatal intensive-care units: A consensus recommendation from Chicago, US
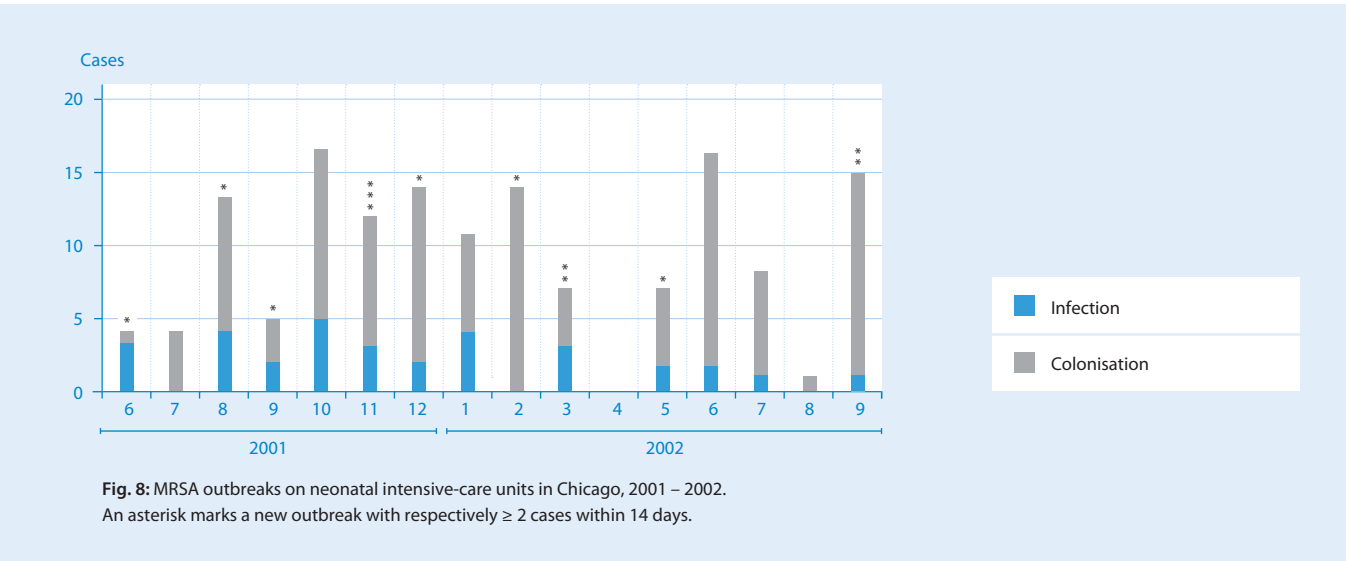
In the US, methicillin-resistant *Staphylococcus-aureus* strains (MRSA) repeatedly cause outbreaks of colonisations and infections on neonatal intensive-care units. Especially with newborns, dramatic courses with deaths can occur very rapidly. After several MRSA accumulations of this kind had been reported to the local health authority in Chicago, a group of paediatricians and hygienists prepared a consensus recommendation in cooperation with the regulatory authorities to prevent and fight such outbreaks.

The working group included clinically responsible physicians as well as hygiene professionals from 9 neonatal units of the highest care level in Chicago. It was called in and coordinated by the staff members of the health authority.

The participating department had on average 38 (scattering range 10 – 48) beds. The working group has met on a regular basis since 2002 in order to exchange clinical experience made

when managing MRSA cases as well as the results of molecular typing of MRSA cases.

As far as possible, all MRSA isolates from the participating hospitals were sent to a central laboratory of the Public Health Service. There, typing was performed by means of pulsed field gel electrophoresis (PFGE). Moreover, literature data as well as already existing recommendations on MRSA management of the Society for Healthcare Epidemiology of America (SHEA, *www.shea-online.org*) were analysed to prepare the consensus recommendation. The recommendations were classified according to the categories of the Centers for Disease Control and Prevention (CDC). First of all, the working group prepared a retrospective overall picture of the outbreak situation between June 2001 and September 2002. During this period of time, MRSA was isolated from 149 children (Fig. 8).

Fig. 8: MRSA outbreaks on neonatal intensive-care units in Chicago, 2001 – 2002.
An asterisk marks a new outbreak with respectively ≥ 2 cases within 14 days.

About one fifth of the cases were invasive MRSA infections, the rest of the cases were colonisations. In the Figure, the respective newly observed outbreaks in a neonatal unit are marked with an asterisk. In this context, an outbreak was defined as the occurrence of ≥ 2 cases within 14 days with strains with the same type of pulsed field. Six of the 31 children who contracted invasive infections died (mortality 19 %). Molecular typing showed

that MRSA clones, which were also identified in other participating clinics, were present in 6 hospitals. Thus, it was obvious that MRSA were spread via transferrals between the clinics.

The group's prepared guidelines on hygiene are compiled in Table 7. Basically, they include the traditional recommendations, already compiled in the SHEA Guideline for adults.

Table 8: Consensus recommendation of the working group on hygiene management

Field/Category of recommendation	Recommendation
Hand hygiene IA	An alcoholic hand disinfectant should be easily accessible close to the patient. Hand washing is only recommended in case of visible soiling.
IA	Regular auditing of hand hygiene with feedback.
Accommodation in cohorts and isolation IA	Affected children should be accommodated in cohorts in a separate room or area. Care utensils and consumables for the children should be stored there separately from those intended for other children.
IA	Entering the cohort area only with gowns and gloves on; this also applies to the rounds.
IA	Masks (protection of mouth and nose) are only required in case of aerosol-induced measures.
Unsolved question	**Collection and transport of waste from the cohort area are performed according to the decision of the local hygiene staff.**
IA	As far as possible, separate nursing staff should be responsible for the children accommodated in cohorts. This should also apply to other medical staff, as far as possible.
II	If no separate nursing staff is available, the nursing staff should first look after the children without MRSA colonisation and then after the children colonised with MRSA.
II	Limited access: As few persons as possible should access the isolation/cohort area.
II	Accommodation in cohorts should be maintained until the last colonised child can be discharged from hospital.
Surveillance cultures IB	Smear tests for MRSA should periodically be performed on children on the neonatal intensive-care unit. If MRSA cases accumulate, the screening frequency should be increased (e.g. to 1 x a week). If the number of cases decreases, it can be reduced again (e.g. to 1 x a month).
IA	Nose and nasopharynx smears are sufficient for the screening.
Screening of staff members IB	Smear tests on staff members are only to be specifically performed if epidemiologic observations point out to a certain staff member to have caused an MRSA accumulation.
Decolonisation treatment IB	According to the decision of the local physicians, Mupirocin can be used to decolonise children and staff members.
Surrounding cultures IA	Corresponding smear and surface tests are only to be specifically performed if epidemiologic observations point out to a certain inanimate source to have caused an MRSA accumulation.
Communication II	Open communication between regional neonatal departments on MRSA management, occurrence of MRSA cases and MRSA status of transferred children or children admitted from other facilities.
Hygiene monitoring IA	The hygiene staff members should audit the compliance of regulations on hand hygiene and other measures of hygiene.
II	The hygiene professionals shall keep the duty rosters of the medical staff and pay attention to whether MRSA accumulations are associated with the presence of certain staff members.

CDC categories (shortened):   IA – absolutely recommended based on very good clinical studies;

IB – absolutely recommended based on clinical studies and theoretical considerations;

II – recommended based on indicative studies and theoretical considerations.

The authors [17] underline the particularity of neonatal departments compared with adult intensive care units. Neonatal units often do not dispose of single rooms, but look after their patients in open bed bays or larger rooms. This results in the necessity to declare a certain 'area' as the cohort area for accommodation in cohorts. In this case, the recommendation to store the required accessories for all MRSA-infected patients separately from the utensils for other children is very useful. Frequent occurrence of MRSA problems with multiple smaller and bigger outbreaks is typical of hospitals in US metropolises. In Germany, MRSA accumulations of this kind are more of an exception on neonatal intensive-care units.

Should they however occur, these recommendations can be very well adopted for events of this kind. Unfortunately, the recommendation does not include any concrete statement on gowns. Here, it should be added that gowns should only be used as long-sleeved gowns (textile or disposable material) with armbands. The restrictive statement of the authors on smear tests on staff members and surroundings, which should only be performed in very concrete suspicious facts regarding a certain source, is most welcomed.

17. New strategies to restore sensitivity to antibiotics of resistant pathogens

As resistances to antibiotics are merely the negative imprint of the use or misuse of antibiotics in a clinic, a restrictive policy on antibiotics is an essential factor to restore a normal sensitivity pattern. The extensive use of cephalosporins of the third generation in some American clinics correlated significantly with the increase in resistant enterobacteriaceae, especially of pathogens of the enterobacter group [13].
To replace the cephalosporins, which exert a strong resistance pressure, different modern extended-spectrum penicillins with inhibitor protection, such as piperacillin/Tazobactam, were used in published studies.
After one-year application of the last-mentioned combination for the initial therapy, rates of resistance, for example, could be reduced by more than 50 % for cephalosporins.
Similarly, the occurrence of vancomycin-resistant enterococci at the US-American East coast correlated especially with the increased use of oral vancomycin.
After introducing a strict prescription policy for vancomycin, rates of resistance dramatically decreased. The use of carbapenems should be controlled and limited in the same manner.

According to [14], the programs for controlled and restrictive use of antibiotics should best include the following steps:

1. regular trainings and further education of medical staff, e.g. through a subcommittee (to the pharmaceutical commission) in charge of antibiotics,
2. regular internal evaluations of the antibiotic resistance of important pathogens,
3. intensive hygiene trainings.

In contrast, introducing a written practice of requirements for certain antibiotics rather leads to increased bureaucracy and not necessarily to success, according to the author. An additional option is possibly a rotating use of different antibiotic initial regimes, e.g. at an interval of three or six months.
Some other possibilities refer to basically use two active substances in the therapy of systemic Pseudomonas infections, preventing the administration of oral quinolones for long-term infection prophylaxis in a clinic, preventing a routine use of substances causing heavy biliation (increased selection pressure in the intestinal tract), as well as preventing regimes involving double β-lactam (β-lactamase induction through cephalosporin partners).

Additional literature

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Author

Hardy-Thorsten Panknin
Specialist Journalism Medicine and Congress Management
Badensche Straße 49 | D-10715 Berlin
e-Mail: ht.panknin@berlin.de

Prof. Franz Daschner, MD, Freiburg, Germany
dedicated to his 70th birthday.

schülke worldwide:

Austria
Schülke & Mayr Ges.m.b.H.
1070 Vienna
Phone   +43-1-523 25 01 0
Fax   +43-1-523 25 01 60

China
Schülke & Mayr GmbH
Shanghai Representative Office
Shanghai 200041
Phone   +86-21-62 17 29 95
Fax   +86-21-62 17 29 97

France
Schülke France SARL
94250 Gentilly
Phone   +33-1-49 69 83 78
Fax   +33-1-49 69 83 85

Germany
Schülke & Mayr GmbH
22840 Norderstedt
Phone   +49-40-521 00 0
Fax   +49-40-521 00 318

Italy
Schülke & Mayr Italia S.r.l.
20148 Milano
Phone   +39-02-40 21 820
Fax   +39-02-40 21 829

Malaysia
Schülke & Mayr (Asia) Sdn Bhd.
47301 Petaling Jaya, Selangor
Phone   +60-3-78 85 80 20
Fax   +60-3-78 85 80 21

Netherlands
Schülke & Mayr Benelux B.V.
2032 HA-Haarlem
Phone   +31-23-535 26 34
Fax   +31-23-536 79 70

Poland
Schulke Polska Sp. z o.o.
01-793 Warszawa
Phone   +48-22-568 22 02-03
Fax   +48-22-568 22 04

Singapore
Schülke & Mayr (Asia) Pte. Ltd.
Singapore 768767
Phone   +65-62-57 23 88
Fax   +65-62-57 93 88

Switzerland
Schülke & Mayr AG
8003 Zurich
Phone   +41-44-466 55 44
Fax   +41-44-466 55 33

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