

Successful control of MRSA spread in Dutch Hospitals

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Abstract

Due to intensive use of antibiotics, strains of *Staphylococcus aureus* have acquired resistance against several antibiotics. Methicillin resistant strains of *S. aureus* are becoming increasingly frequent worldwide and are associated with higher mortality, longer admissions and larger hospital expenses. In response to this worldwide trend, Dutch hospitals have adopted the search-and-destroy policy. In accordance to this policy, patients with MRSA are rapidly isolated and treated until the infection or colonization has been eradicated. These measures, together with the culturally determined low use of antibiotics in the Netherlands, have lead to one of the lowest prevalences worldwide. This article discusses the most important measures in the Dutch protocol.

Introduction

Staphylococcus aureus are gram-positive bacteria that are frequently present on the skin and mucous membranes. *S. aureus* has developed resistance against several antibiotics and is termed MRSA (methicillin-resistant *S. aureus*) when it is resistant against methicillin and other β -lactam antibiotics. MRSA is frequently present in hospitals due to high selection pressure because of frequent use of antibiotics and beneficial conditions for spreading throughout the

hospital, for instance via hands of medical personnel.¹ Infections with *S. aureus* can manifest as endocarditis, impetigo, arthritis and in some cases pneumonia.² MRSA is increasingly present in hospitals worldwide and is a significant healthcare risk. For dealing with this development, hospitals in the Netherlands have adopted a unique protocol that, together with the culturally determined limited use of antibiotics, has lead to a low prevalence of MRSA in Dutch hospitals.

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Virulence

Resistance of *S. aureus* against antibiotics is determined by a gene that does not include any additional virulence factors. Research into the types of toxins produced by methicillin-sensitive and methicillin-resistant *S. aureus*, has shown no differences between these two.³ Outcomes of infection with these either sensitive or resistant *S. aureus* do differ. Compared to pneumonia caused by methicillin-sensitive *S. aureus*, pneumonias caused by MRSA are associated with increased time on mechanical ventilation and increased incidence of organ damage.⁴ Research into outcome of bacteremia concluded that infections with MRSA are associated with a higher mortality rate.⁵ Bacteremias caused by MRSA are also associated with a longer stay in hospital and higher medical expenses.⁶ These outcomes can most likely be attributed to other factors than additional virulence factors. Patients infected with MRSA are significantly older. Moreover, before treatment with vancomycin (which is the first choice treatment for MRSA) can be given, confirmation of infection with MRSA has to be done, which results in treatment delay.⁴ It is also believed that vancomycin might be less effective clinically than flucloxacillin, which is the first-choice treatment for methicillin-sensitive *S. aureus* infection.

Low prevalence of MRSA in the Netherlands

After the introduction of methicillin in 1959, resistance against this antibiotic was soon reported. In 1961, a case was reported in Great-Britain of an infection with *S. aureus* that did not respond to methicillin.⁷ In the following years, similar cases were reported from United States, Japan and Australia. Methicillin resistance has become an increasingly large problem in these countries. In the United States, the percentage of hospitals with reported cases of MRSA has risen from 2,4% in 1975 to 29% in 1991⁸ and 46% in 2000.⁹ Hospitals in the Netherlands have a significantly lower prevalence of methicillin resistance.

One percent of blood isolates of *S. aureus* in Dutch hospitals are MRSA (<http://www.rivm.nl/earss/>). Systematic surveillance for methicillin resistance was started in 1989. Before this time, incidental cases of MRSA were reported. Since then, the prevalence

of MRSA in the Netherlands has stayed more or less constant. Aside from the low prevalence of MRSA in blood isolates, the number of people with asymptomatic nasal carriage of this bacterium is also low (0.03%),¹⁰ which makes the Dutch prevalence of MRSA one of the lowest in the world. This low prevalence is due to the restricted use of antibiotics and the search-and-destroy policy that is currently used in the Netherlands.

Search-and-destroy policy in the Netherlands

Limited use of antibiotics in the Netherlands is principally culturally determined and has not been established specifically to withstand the emergence of MRSA. Research into the frequency of antibiotic use outside of hospital in the European Union, has shown that antibiotic use in the Netherlands is particularly low. When determined as 'defined daily dose' per 1000 persons per day, it is currently 8.9.¹¹ This is the lowest in Europe, especially compared to France (36.5), Spain (32.4) and neighboring country Belgium (26.7).

In contrast to the low consumption of antibiotics, the search-and-destroy policy has been specifically introduced to counteract the emergence of the resistant bacteria and MRSA in particular. It was introduced as soon as cases of methicillin resistance were reported, although the first official protocol was written down in 1989. The search-and-destroy policy implies that, when an infection with MRSA is suspected or diagnosed, strict measures are taken. Patients with an increased risk of MRSA colonization include patients that were hospitalized abroad for more than 24 hours in a period of 2 months before admission, foreign dialysis patients and patients that shared a room with an MRSA positive patient, amongst others (so called category 2 risk). These patients are directly isolated. The same holds for patients who have contact with living pigs or calves, because MRSA carriage is high among these patients. If cultures come back negative, no further action is taken. When cultures come back positive (category 1), the bacteria are to be eradicated.¹² Patient isolation is subject to strict measures. An airlock is mandatory to prevent airflow spreading MRSA throughout the hospital. Medical personnel are obliged to use masks, gloves and gowns with long sleeves to prevent intensive skin contact.¹³ The number of people providing care

for the patient is limited as much as possible without compromising optimal care. These measures are abolished if the bacteria are eradicated. This is the case when three consecutive cultures are negative (with an interval of one week between cultures). Patients with a moderately increased risk of MRSA colonization (category 3) include Dutch patients that have undergone hemodialysis abroad or patients that have had positive cultures in the past. These patients are screened on admission but are not hospitalized in isolation while the result of the cultures is awaited.

Medical personnel that suffer from skin conditions like eczema or psoriasis can not be a part of the treatment team of a patient with MRSA, because they are at a greater risk of becoming colonized by resistant bacteria and are more difficult to treat. Hospital employees that have had unprotected contact with (unexpected) MRSA positive patients (category 2 risk) are screened and prohibited from returning to work. If cultures are positive (category 1), these employees are treated and can only return to work when a second culture come back negative. Employees with skin abnormalities are screened for a longer period of time and return to work if three consecutive cultures are negative (with a period of 5 days between cultures). Personnel that have had contact with MRSA positive patients in conformity with the search-and-destroy protocol (category 3 risk) are tested for MRSA colonization, but can resume their work before cultures come back. Medical personnel that have worked abroad during the past 2 months or on a regular basis are also regarded as having a category 3 risk of colonization and are treated accordingly. All measures can be found on the website of Dutch working party on Infection Prevention (www.wip.nl). These measures might seem very costly, but are indeed cost-effective. If MRSA was more frequent in the Netherlands, expenses would be significantly higher due to increased use of antibiotics.¹⁵ Great Britain used to have a similar system, but deserted this protocol in 1995 because many hospitals did not have sufficient accommodation to comply with these measures.^{16,17}

Treatment of MRSA in the Netherlands is done in cooperation with infectious disease specialists. First choice treatment is currently vancomycin. Because of *S. aureus's* ability to develop resistance for antibiotics, the first cases of vancomycin-resistant MRSA have already been reported.¹⁸ Maintaining the search-and-destroy policy is an effective measure to prevent this development in the Netherlands for as long as possible.

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