ReAct facts

A fact sheet from ReAct – Action on Antibiotic Resistance, www.reactgroup.org

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Burden of Resistance to methicillin-resistant *Staphylococcus aureus*

◆ *Staphylococcus aureus* is a common cause of serious infections, including blood stream, respiratory, bone and joint infections. Antibiotic resistance emerged many years ago, and methicillin-resistant *S. aureus*, MRSA, is now a common pathogen worldwide. Such resistance makes many common antibiotics useless and infections difficult to treat adequately. As a consequence MRSA has become a significant burden on individual patients, on healthcare, and on society, with substantially increased length of hospital stay and costs as well as increased risk of fatal outcomes.

◆ Mortality almost doubles when MRSA is the cause of bacteremia compared with infection caused by sensitive strains, MSSA. Until quite recently infections have occurred in hospitals or in settings with a clear hospital association and have usually affected patients with serious underlying conditions.

◆ Lately, different strains with no such association have emerged in the community. These community-associated strains, CA-MRSA, often affect younger, healthier people, sometimes with fatal outcomes in the case of pneumonia, in the absence of timely and appropriate treatment.

SCOPE OF THE PROBLEM

Staphylococcus aureus

☐ One of the most important bacteria causing human disease and death

☐ Leading cause of hospital-acquired infections [1,2]

☐ Major cause of skin, soft tissue, respiratory, bone, joint and endovascular infections. A large proportion of these, other than skin infections, require systemic antibiotic therapy and hospital care. A small proportion of patients may experience severe, life-threatening infections such as blood stream infection or pneumonia, with potentially fatal outcomes.

☐ 20% to 30% of the entire human population is colonized by *S. aureus*, without symptoms or signs of infection. In a population-based survey performed in the United States, the prevalence of colonization with *S. aureus* was 31.6%. [3]
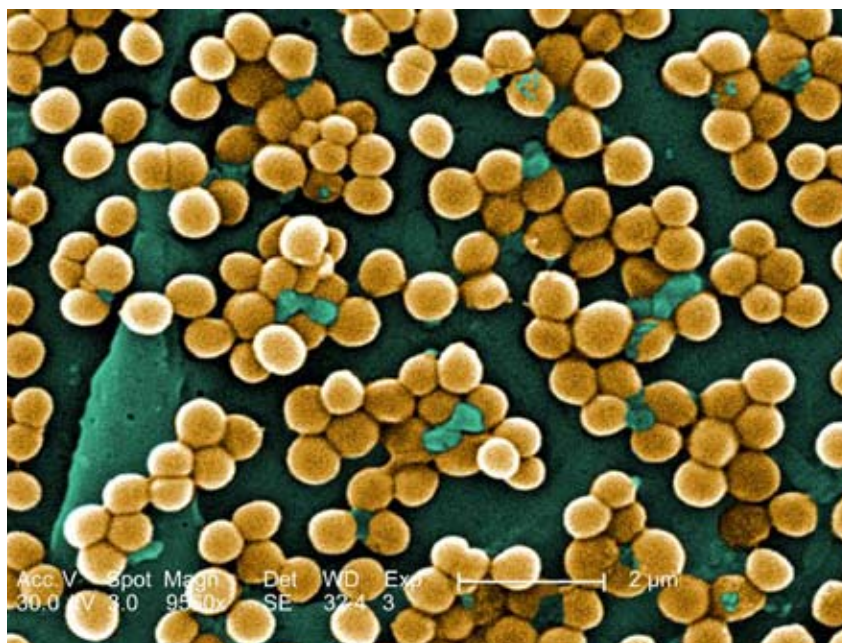
Methicillin-resistant *Staphylococcus aureus* bacteria.
Photo: Public Health Image Library

Methicillin-resistant *S. aureus* (MRSA)

- Worldwide problem, adding to the overall burden of infectious diseases.[2]
- Surveillance data have shown an increasing incidence of MRSA infections in many countries. [4]

Community-associated methicillin-resistant *S. aureus* (CA-MRSA)

- Has emerged as an important pathogen in recent years. [5,6]
- Outbreaks in healthy children and adults have been reported worldwide.
- Most often causes skin and soft tissue infections, but other more serious infections can occur, such as necrotizing pneumonia.
- CA-MRSA strains are genetically different from health-care associated strains (HA-MRSA).
- In contrast to HA-MRSA, CA-MRSA is usually sensitive to many antibiotics, although not to beta-lactam agents.

DEFINITIONS

HA-MRSA (Health-care associated MRSA)

- Infections where onset occurs after 48-72 hours of hospitalization
- Infections in patients with significant previous healthcare exposure during which they may have acquired MRSA colonization, e.g:
- recent hospitalization
- surgery
- dialysis
- residence in long-term care facility
- indwelling devices
- previous history of MRSA infection or colonization.
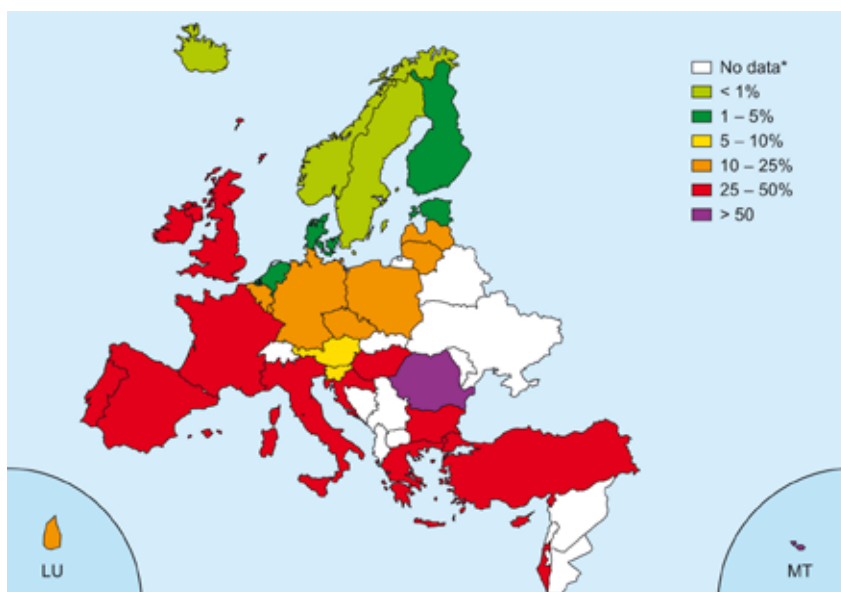
MRSA in Europe 2006. *S. aureus:* Proportion of invasive isolates resistant to oxacillin (MRSA) in 2006. *These countries did not report any data or reported less than 10 isolates
Source: http://www.earss.rivm.nl, March 2008
However: true population-based estimates of the prevalence and incidence of healthcare- and community-acquired MRSA are lacking for many countries.

CA-MRSA (Community-associated MRSA)

- Infection with onset in the community or within 48-72 hours of hospitalization and where the risk factors mentioned above are not present.

EPIDEMIOLOGY

In contrast to temporary outbreaks, MRSA is considered endemic in hospitals when

- at least 20% of all *S. aureus* isolates are MRSA
- prevalence of MRSA carriers at admission is >1% of patients outside of the Intensive Care Unit (ICU) and >5% inside the ICU setting
- incidence of MRSA carriage is 0.5 or more new cases per 100 admissions.

TREATMENT OPTIONS FOR HEALTH-CARE ASSOCIATED INFECTIONS

- Glycopeptides, currently available first-line antimicrobial agents, have inferior efficacy compared with antibiotics used for treatment of sensitive strains, especially if given in low dosage.
- Resistance to glycopeptides (vancomycin intermediate sensitive/ resistant *Staphylococcus aureus*, or VISA/VRSA) has already been described.
- Alternatives either very expensive (linezolide) or less effective(cotrimoxazole) or insufficient data available to promote their use (rifampicin & fusidic acid or doxycycline).

QUALITATIVE CONSEQUENCES OF RESISTANCE

Individual effect

- ☐ Increased risk of infection on admittance to high-prevalence hospitals (e.g. for surgery)
- ☐ Treatment failure due to wrong choice of medicine or dosage
- ☐ Treatment more 'troublesome' for patients due to the need for hospitalization in the absence of oral treatment alternatives and the need to monitor treatment.
- ☐ Use of more toxic alternatives; risk of serious adverse reactions
- ☐ Increased morbidity and mortality
- ☐ Especially high impact in patients undergoing hemodialysis or transplantation and in patients with other serious underlying diseases, e.g. diabetes

Institutional impact

- ☐ Difficult & time-consuming cooperation between healthcare providers
- ☐ Disruption of care
- ☐ High costs of benchmarking and mandatory declaration (e.g. France, UK) with public reporting
- ☐ Increased costs of empiric and directed antibiotic treatment
- ☐ Infrastructure costs of effective surveillance programs

- ☐ Increased hospitalization for non-severe infections due to the lack of orally available drugs
- ☐ Bad hospital reputation, loss of confidence.

Societal impact

- ☐ Effects on families & communities due for example to high costs of care and/or decreased incomes and tax revenue if patients are unable to work
- ☐ Increased overall healthcare expenditures
- ☐ Loss of finite societal resource (antibiotics): future generations will not be able to benefit from active antibiotic treatment
- ☐ Out-of-hospital, indirect and intangible costs including physical and psychological costs .

QUANTITATIVE CONSEQUENCES OF RESISTANCE

Most studies relating MRSA infections to specific patient outcomes (deaths, lengths of hospital stay, costs) have been conducted in North America. Most data may not be generalizable to other countries.

- ☐ CDC estimates based on studies in the US[8,9,10]: at least 126,000 patients infected by MRSA, at least 5,000 die of these infections and at least US$ 4 billion of extra costs each year
- ☐ Despite effective treatment mortality due to MRSA bacteremia is still 10-40%, with an increased risk of mortality for patients not treated adequately [3]
- ☐ MRSA bacteremia associated with significantly higher mortality than is MSSA bacteremia (OR. 1,93; 95 %CI 1,54-2,42; P< .001) [11]
- ☐ MRSA mortality rates increased over 30-fold during the period 1993-2006 in the UK.[12]
- ☐ Increased direct costs of providing care: US$ 2,500–27,000 (though this is probably an overestimate due to methodological pitfalls) [3,7]
- ☐ SCORE report 2004 (very crude analyses): Cost of 120 million due to Health-care associated MRSA bacteremia in Europe.
- ☐ 1,277 additional fatal cases due to MRSA in Europe.

PERSPECTIVES

Urgent needs

- ☐ A sound methodology for estimating, on a country-by-country basis, the mortality, burden of disease and economic burden arising from MRSA (including CA-MRSA). Important not to overestimate direct costs and underestimate indirect costs.
- ☐ Methodological improvements (time-to-event data analyses).

A dark scenario

- ☐ MRSA resistant to all available antibiotics.
- ☐ Pandemic flu scenario; secondary pneumonias will be difficult to treat if caused by CA-MRSA (highly virulent and lethal).
- ☐ No prospect of *S. aureus* vaccine for broad use.
- ☐ New epidemic strains causing CA-MRSA infections most likely to become endemic around the globe, and multiresistant (already described in the US and Algeria).
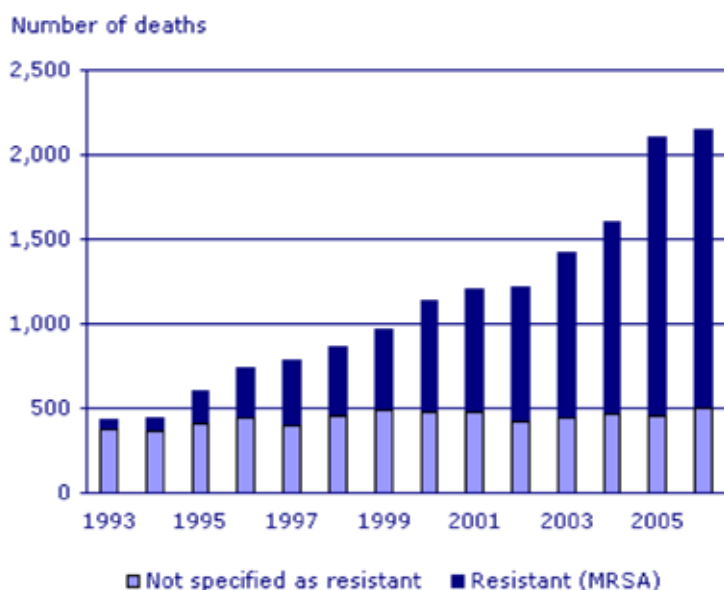
Number of death certificates with MSSA/MRSA as underlying cause of death (UK)
Source: http://www.statistics.gov.uk, March 2008

SUGGESTIONS FOR FURTHER READING

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12. Number of death certificates with MSSA/MRSA as underlying cause of death (UK), http://www.statistics.gov.uk, March 2008