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Controlling methicillin resistant *Staphylococcus aureus*

Time to return to more stringent methods of control in the United Kingdom?

See also p 1209

Methicillin resistant *Staphylococcus aureus* (MRSA) is a major cause of hospital acquired infection worldwide, posing a growing threat to public health. It belongs to a species of ubiquitous and versatile organisms that are continually adapting to new antimicrobial and environmental challenges, often through gene transfers even from distantly related organisms such as vertebrates. Why is MRSA important? Some strains are eminently transmissible, resulting in large numbers of infections in hospitals. Bacteraemia data for England and Wales show that MRSA as a proportion of total *Staphylococcus aureus* bacteraemias rose from under 2% in 1990 to 42% in 2000[1 2]—one of the highest reported rates in Europe.

Methicillin resistance was first reported in 1961 shortly after the introduction of methicillin (similar to flucloxacillin), the first penicillin resistant to destruction by staphylococcal β-lactamase. The discovery of methicillin was an important development as many hospital strains of *S aureus* had become penicillin resistant in the 1950s through the production of β-lactamase.[w1] Some European countries experienced problems with MRSA in the 1960s, but this was followed by a period of declining incidence of multiple antibiotic resistance in *S aureus*.[w2] However, in the 1980s MRSA returned, with the advent of new strains with epidemic potential (epidemic MRSA or EMRSA). These have been numbered sequentially in the United Kingdom, where three have dominated: EMRSA-1, prevalent in the Thames regions in the 1980s and probably originating in Australia, and EMRSA-15 and 16, which are currently predominant in the United Kingdom and responsible for outbreaks elsewhere.

Evolutionary studies suggest that most MRSA strains are derived from a few clones, arising separately by integration of the *mec*A gene responsible for methicillin resistance into different strains of methicillin susceptible *S aureus*. This gene is located on a novel genetic element, the staphylococcal cassette chromosome *mec*.[3] Glycopeptide antimicrobials, notably vancomycin, are the mainstay of treatment of MRSA infections, although recently introduced agents such as synercid and linezolid have a role. However, intermediate and full resistance to vancomycin have now been described, as has resistance to newer agents.[4 5]

MRSA infections are additional to the burden of methicillin susceptible *S aureus* and have serious sequelae. Crowcroft et al showed increasing mortality from MRSA in England and Wales paralleling the increase in bacteraemias.[6] MRSA can carry virulence factors found in methicillin susceptible *S aureus*, as shown in reports of MRSA associated toxic shock syndrome, whereas infections with strains containing Panton-Valentine leucocidin recently came to prominence for causing serious skin infections and necrotising pneumonia in the community.[7] Furthermore, MRSA infections may be difficult to treat as there are reduced antimicrobial options; in addition, some of the agents can be difficult to administer, have side effects, and may not penetrate particular body compartments well—for example, in the treatment of bone infections or endocarditis. Also, the available agents may not be as effective against MRSA as standard agents are against methicillin susceptible *S aureus*. The cost of treatment and extended admissions result in sizeable extra costs to health services.

Reports of community acquired MRSA from several countries denote a worrying development. One such report described paediatric deaths.[8] The causative strains often differ from hospital ones and seem to have arisen independently in the community. Treatment and control can pose big challenges in some situations—for example, an outbreak of MRSA containing Panton-Valentine leucocidin in a prison. In the United Kingdom, the indications are that MRSA is a pathogen that is still predominantly acquired in hospital, although export of these strains may generate problems in the community—for example, in residential and nursing homes.

Much debate surrounds the control of MRSA. Little doubt exists that robust control of infection is needed and that the foundation for this is hand washing by healthcare staff. However, numerous publications have shown that despite maximal efforts it is difficult to get this beyond 60-70%, and few well designed studies have assessed the relative contribution of additional control measures. A recent systematic review of the effectiveness of isolation measures indicated that concerted efforts that include isolation could reduce MRSA even in endemic settings.[9] Three sets of guidelines have been published to cope with the growing problem of MRSA in the United Kingdom since the 1980s. These started off with a rigorous "search and destroy" approach, based on screening of patients and staff and isolation of affected patients. These were modulated under the pressure of increasing incidence—against a background of poor support from senior management, lack of isolation facilities, high occupancy rates of beds, and understaffing—into a more targeted approach.[w3 w4] The latter focused on controlling MRSA in high risk areas, such as cardiothoracic surgery units, with the recommendation

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Additional references w1-w4 appear on bmj.com

BMJ 2003;327:1177–8

that referral centres should screen patients on admission to the unit and transfer from affected wards.

The United Kingdom now has some of the highest rates of MRSA infection in Europe, and the control of healthcare associated infection is a priority for the government. Acute hospitals have been required to implement mandatory surveillance of *S aureus* bacteraemias, and results from individual hospitals have been incorporated into the national hospital performance indicators, published recently.[10] Countries that seem to have been successful in controlling MRSA have largely used the search and destroy approach, and recent American guidelines are advocating a similar approach.[11 12] The government focus on healthcare associated infection indicates that a more stringent approach in England now has high level support. The MRSA working party has been reconvened to update the 1998 guidelines in the light of recent developments.[w4]

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Trauma life support in conflict

Resources must be optimised for the many, rather than dispersed for the few

War injures and kills combatants and civilians. Medical resources are usually scarce in combat zones, and doctors must plan to make the most of these resources to minimise death and suffering. Planners seek to apply the widely adopted principles of advanced trauma life support to the treatment of penetrating wounds, burns, and other forms of acute physical trauma on the battlefield. This recognises the critical importance of effective early resuscitation after wounding to minimise the consequences of shock and to improve survival.

Mortality after civilian trauma has been described as having a trimodal distribution.[1] The first peak of deaths occurs within minutes of the event from non-survivable injuries, even with the most advanced medical resources immediately to hand. The second peak may account for some 30% of deaths, in the first few hours after injury. Death is most often due to hypoxia and hypovolaemic shock.[2] This group stands to benefit the most from excellence in trauma care. The third peak, of up to 20% of trauma deaths, occurs late after the injury, from sepsis, multi-organ failure, and other complications.

Does this descriptive model help the allocation of resources for trauma care in a war? Much severe civilian trauma is blunt, arising from road traffic accidents rather than from penetrative fragments and bullets, blast, and burns. The circumstances of war also differ from peacetime casualty incidents in that communications are often poor, the environment dangerous, and recovery teams and routes of evacuation unsafe and unreliable. Circumstances differ hugely from one conflict to another and even within individual war zones. Rapid treatment and evacuation of casualties to definitive care undoubtedly improves survival.[3 4] However, other than for the lucky few, the evacuation of casualties to hospital usually takes hours,[5] even in advancing forces with full and secure helicopter and road transport.[6] A delay of several days is often seen by surgeons working for the International Committee of the Red Cross.[7 8]

One possible solution to the problem of how to optimise trauma care on the basis of modern principles of advanced trauma life support is to disperse resuscitative surgical teams widely around the war zone to bring care forward to casualties. This has led to the development of the concept of "damage control surgery," and surgical teams are co-located with mobile stations that receive casualties.

Unfortunately in such relative isolation such teams cannot work to best effect. The resuscitation and immediate aftercare of patients who may have multiple penetrating, blast, and burn wounds require complex multidisciplinary teamwork. This includes a high standard of resources to support high dependency and intensive care and a holding capability for postoperative patients pending safe and stable evacuation or definitive corrective and revision surgery. Forward trauma teams, which are obliged to undertake

BMJ 2003;327:1178–9