Outbreak Column 13: Nosocomial *Staphylococcus aureus* outbreaks (part 2 – guidelines)

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In Outbreak Column 12 I presented a brief history of nosocomial *Staphylococcus aureus* outbreaks from the 1950s to the emergence of the epidemic methicillin-resistant (MRSA) [the older term 'methicillin' is used throughout this column to avoid confusion] strains of the 1980s (Curran, 2014). Outbreak Column 12 touched on the period in the 1940s before the organism was first recognised as a nosocomial pathogen. Noted in the column was the inability to control these organisms because of the inadequate healthcare environments and some healthcare practices therein. Also noted was the periodic decline of epidemic strains such as occurred in the 1970s (Curran, 2014). Outbreak Column 13 focuses on guidelines from the 1980s onwards which were produced for infection prevention and control teams (IPCTs) to use to prevent outbreaks of (and hospitals becoming endemic with) MRSA. As IPCTs are already embarking on our next major challenge, the control of carbapenemase-producing enterobacteriaceae (CPE), it is an opportune moment to take stock and muse. This Outbreak Column is therefore a reflection, with acknowledged hindsight bias, from an infection control practitioner who over the 25 years has tried to implement each of the guideline iterations. This review has resulted in a personal consideration of what I would do differently if the situation was repeated.

Evolution of guidelines aiming to control *Staphylococcus aureus*

UK guidelines for the control of staphylococci have been updated periodically since they were first produced in 1959 (Anon, 1986, 1990, 1998; Coia et al, 2006). Table 1 lists the guideline titles, the number of pages and the time between productions. Each new guideline increased in size from the previous version although the number of topic areas did not itself alter much. What is noticeable from the titles at least is that the 1986, 1990 and 2006 guidelines are attempting to control the organisms; and only the 1959 and 1998 guidelines are explicitly trying to control infections. It is possible that the authors considered that controlling organism transmission was synonymous with controlling infection – this will be further examined later. It is not until the 2006 guidelines that the word 'prevention' appears in the title. Latterly in 2008, guidelines were produced to prevent and control infections caused by *S. aureus* – not specifying a resistance pattern – but the possession of the Panton-Valentine Leucocidin toxin; this guidance is not covered in Outbreak Column 13.

1986

The 1986 guidelines were produced for the control of epidemic methicillin-resistant *Staphylococcus aureus* (EMRSA) (Anon, 1986). There

were no specific recommendations for methicillin sensitive *Staphylococcus aureus* (MSSA; Anon, 1986). The authors, under the chairmanship of Professor Ayliffe, cited reasons for the guidance, which included: the extensive spread of EMRSA had happened very quickly, treatment of patients with multi-resistant strains was difficult and control had required extraordinary measures (Anon, 1986).

The approach within the guidance for EMRSAs was almost a one-size-fits-all as emphasised by the measures to be taken if there was more than one case identified in a ward:

"All other patients and staff must be screened and isolated and treated if any samples are positive. Medical, nursing, paramedical (particularly physiotherapists and phlebotomists) and domestic staff should be screened. It may be necessary to close wards to new admissions, particularly to surgical or intensive care patients." (Anon, 1986)

This was certainly a control measure that could bring health care to an abrupt halt. It would seem reasonable to conclude that the assumption behind this recommendation was that significant transmission occurred from both recognised and unrecognised carriers, and that all colonised persons could be identified, isolated and decolonised. However, later on in the text the authors indicate that there was little or no expectation of successful carrier eradication of EMRSA (and thereby control of the spread of the organism). Despite the 'screen all' policy, comments in the decolonisation section stated that 'eradication of carriage is difficult and may often fail'. There is something illogical here given that such efforts were taken to find carriers yet eradication methods were considered so unlikely to succeed. What was highlighted as being of paramount importance to limiting the spread of EMRSA was the isolation of infected or colonised patients who were transferred from affected hospitals. The guidance stressed that MRSA control would be further aided by the restriction of inter-hospital movements (Anon, 1986).

There were no recommendations included in the 1986 guidelines to control antibiotic consumption or involve and engage with anyone else to promote the required actions. This was clearly a task the IPCT had to do by itself.

With hindsight the 1986 guideline was doomed to fail for several reasons. For example, significant geographical spread throughout the UK had already occurred, and also the way hospitals worked facilitated the spread of these organisms, i.e. there was insufficient isolation facilities, frequent inter- and intra- transfer of patients, significant staff movement between clinical areas, and it took days to identify

Table 1. The production of UK guidelines to prevent and control staphylococi in healthcare settings (time since previous production)

		Pages
1959	Staphylococcal infections in hospitals	36*
1986	Guidelines for the control of epidemic methicillin-resistant <i>Staphylococcus aureus</i> (27 years)	9*
1990	Revised guidelines for the control of epidemic methicillin-resistant <i>Staphylococcus aureus</i> (4 years)	26
1998	Revised guidelines for the control of methicillin-resistant <i>Staphylococcus aureus</i> infection in hospitals (8 years)	37
2006	Guidelines for the control and prevention of methicillin-resistant <i>Staphylococcus aureus</i> (MRSA) in healthcare facilities (8 years)	44
2008	Guidelines on the diagnosis and management of PVL-associated <i>Staphylococcus aureus</i> (PVL-SA) in England	50

(* these productions were of a smaller page size)

who was and who was not colonised. Consequently, for all their efforts IPCTs were always closing the stable door after several horses had bolted. At that time IPCTs would aim to make the best decisions given the resources available to them. With hindsight, occasions when there was a 'failure to isolate' due to unavailable isolation rooms should have made its way onto some kind of risk register much earlier.

1990

Only four years after the 1986 guidelines were published, the production committee was reconvened to replace them (Anon, 1990). The 1990 guidance states that re-production was necessary because "problems have arisen that were not dealt with in the first report" (Anon, 1990). Although the specifics of these 'problems' were not discussed there was a significant relaxation of the 'screen all' approach that had been advocated in 1986. Screening was now reserved for patients and staff in 'critical areas such as surgical intensive care areas' (Anon, 1990). Of note there was no specification in this iteration as to who was included in the term 'staff'. It was also noted that in a hospital with an endemic problem it may not be 'economically feasible to screen after single isolates'. Note the rationale for 'not screening', i.e. that the hospital might not be able to afford it – efficacy and patient safety arguments were not put forward (Anon, 1990).

There is also an entire new section on the cost implications of MRSA in the 1990 guidance; this suggests the 1986 control measures had failed to keep control of both the organism and the budget. Costs of control of major outbreaks were quoted in one instance as £250k; more importantly the differential antibiotic treatment cost between methicillin-sensitive and resistant strains was £380 (£60 vs. £440 respectively). Also detectable within these 1990 guidelines were other unsolvable problems. Just as the 1959 guidance acknowledged decontamination issues with mattresses and not washing blankets, the 1990 (and 1986) guidelines once again included problems with the inability immediately to identify whether a person had an epidemic strain of MRSA. This is exemplified in the following passage:

'There are many distinguishable strains of MRSA, which may or may not be epidemic. These guidelines deal primarily with epidemic strains although there are no distinguishing features that allow the recognition of such strains on first isolation.' (Anon, 1990)

So these were guidelines for the control of an organism that could not be readily identified but was readily transmitted. At the time it took 48

hours to identify the organism as MRSA – identifying if the MRSA was an epidemic strain took much longer.

During the 1980s and 1990s, there was extensive use of agency nurses in London, and many other city hospitals. This was also a time when many London hospitals were affected by EMRSAs. Of note the agency nurses were required most where the problem was most acute – the intensive care units. The 1986 guidelines had focused considerable efforts on control measures for agency nurses who could work in several different hospitals (endemic and non-endemic) within a week. If one such nurse shed vast quantities of the organism there could be widespread transmission in several hospitals and yet extensive outbreak screening of permanent staff might find no carriers. The guideline writers were concerned that these ways of working were part of the problem. However, one of the 1986 recommendations for agency nurses was, again with hindsight bias, draconian.

'Agency nurses... if it is known they have worked recently in a hospital with colonised or infected patients, special hygiene precautions (e.g. bathing with an antiseptic detergent) may be necessary if insufficient time is available for adequate screening.' (1986)

This recommendation could not be implemented. Agency nurses were not obliged to disclose to employees where they had just worked; and why would they, if as a consequence they would be screened, scrubbed and have some future employment opportunities reduced? Ward managers would have expected agency nurses to have started their shifts promptly – not with a 'see you when you have had a shower'. Although the guidance includes a variety of possible actions for local consideration, in something of a further admission of defeat, or perhaps recognition that there were too many factors for a national guideline to accommodate, this impractical recommendation was changed in 1990 to 'Each hospital should decide the most practical solution' (Anon, 1990).

The 1990 guidance pulled together some very useful practical measures, including isolation practices, examples of decolonisation regimens and prewritten notification letters which were provided as appendices (Anon, 1990). The changes in the 1990 guidelines were designed to ease the unintended consequences of implementation on healthcare systems; in doing so it could be argued they were therefore less likely to achieve control. Expectations of successful decolonisation were still low and there was still an inability to reliably and promptly detect colonised persons. There were still too few side-rooms to enable isolation of patients who were recognised as being at

a higher risk of having MRSA. Even though the healthcare environment had improved markedly since the first guidance in 1959, clinical teams and IPCTs were still doing the best they could with what they had – which was still insufficient to gain control.

These guidelines were focused on minimising transmission. Although there is a section titled 'Prevention of spread of infection between patients' the contents therein were only about preventing transmission – there were no control measures to prevent infections. Local surveillance or epidemiology was extremely primitive at that time and generally not computerised. (In the early 1990s I was able to produce a computer-generated line list, but to do so each morning I had to load DOS on to the computer (one floppy disc), then load the software onto the computer (two floppy discs), then load the file on to the computer (one floppy disc) and only then could I produce one line list (using DOS commands; there was no mouse and no pull-down menus). Little wonder I extolled the virtues of the then new Centers for Disease Control's epidemiology freeware Epi Info (Curran, 1993).

1998

Almost 40 years after the appointment of the first infection control nurse, finally as a body there was an invitation to participate in the revision of the revised guidelines for the Infection Control Nurses' Association (ICNA) (Anon, 1998). The ICNA joined the Hospital Infection Society and the British Society for Antimicrobial Chemotherapy as part of the guideline production working party (Anon, 1998). The working party pointed out that '*in the light of changes in epidemiology, increasing prevalence and finite hospital resources available to control spread there was pressure to re-convene*' (Anon, 1998). I can find no explanation in the guidelines for the dropping of the epidemic 'E' from the title. Reference is made about the requirements for specific MRSA strains to be labelled epidemic, i.e. '*When epidemic strains have spread in two or more hospitals within the UK, they have been numbered sequentially, i.e., EMRSA-1, EMRSA-2, etc*' (Anon, 1998). The 1998 guidelines were, in particular, for the control of two epidemic strains which had emerged to become a significant problem since the 1990s – EMRSA-15 and EMRSA-16 (Anon, 1998).

Having become familiar with looking at the tail of epidemic curves over recent years, for both MRSA and *Clostridium difficile*, it is a little unsettling to go back and look at the left hand side of the curve. At this time the epi curve for new MRSAs was still rising steeply without any sign of a peak or plateau. This is the context in which the great and the good gathered to decide what should be done and be done differently to control these organisms.

For some experts, the spread of MRSA was considered to be potentially the greatest threat to modern medicine (Ayliffe, 1997). However, Ayliffe (1997) also noted that these MRSAs could decline in the way that previous strains had done before. The working party stated:

'They [MRSAs] pose increasing problems in hospitals because of difficulties in treating systemic infection and their propensity to spread and colonise debilitated patients. Consequently, strategies have evolved to minimise spread and prevent infection' (Anon, 1998)

Perhaps therefore this was the theoretical basis for the guidelines – actions focused on preventing transmission would prevent infections. Preventing spread was considered important to reduce the additional costs of treatment and of control. With regard to the cost argument the guidelines now quoted the cost of control of one outbreak at £400k and another at £700k (Anon, 1998). Even though many patients became debilitated and were not initially infected, it has been shown that MRSA colonisation can remain a long-term risk factor for future MRSA infection, particularly for patients with chronic illnesses (Quezada Joaquin et al, 2013).

The debate was still raging as late as 1998 as to whether MRSAs were any more virulent than MSSAs. The working party (1998) concluded that:

"MRSA may be as virulent as MSSA, that control measures do have an impact and that the costs of not controlling are higher than those of control. Control of MRSA is still worthwhile" (Anon, 1998).

There is a marked lack of both certainty and conviction in this statement. It seems illogical that there was no guidance to control MSSA given that it was considered to be possibly more virulent than MRSA. Although arguments against control of EMRSA were noted – possibly the main (and unwritten) reason to persist with attempts at control – which at that time was out of control in many hospitals – was that it would be unethical not to try.

The two previous guidelines (1986, 1990), which had advocated a very strict and then a slightly less strict approach of attempting to find and destroy EMRSA, had proved unsuccessful. Although there were a few reports of local success – there were even fewer UK reports of long-term success. One IPCT found that effective ward closures enabled them to contain multiple outbreaks of MRSA – but ultimately they 'lost the war' (Farrington et al, 1998). A different approach was evidently needed. The main difference in the 1998 guideline was that the decision-making of what was to be implemented had switched from what the guideline writers' specifically advocated, to what the IPCTs locally decided were necessary given all the factors in the healthcare systems they managed. The impracticalities of the inflexible 1986 and 1990 guidelines had resulted in a 1998 approach that again improved the degree to which implementation was now possible – however, it did not improve the extent to which implementation was likely to lead to control of the organism. Once again the authors made no claims that their advocated guidance was likely to be successful in gaining control. Even though 'infection' was included in the title of the document, the 1998 guidelines remained focused on preventing spread and not on preventing infections. There was still no instruction to understand what type of infections MRSA was causing and as a consequence what should be done to prevent what was on the patients getting inside them.

Having set out a stall of 'General Principles' that should always be in place the 1998 guidance then sets out the variables which will determine what the IPCT would advocate locally as the MRSA control strategy. The variables included the ward design, patient population and virulence of the organism if known (Anon, 1998).

This local IPCT risk-based approach remained extant until it was replaced in 2006. Before replacement however, two important interjections had been made. Firstly, mandatory surveillance of MRSA bloodstream infections had been introduced in 2001. Hence the part of the problem that was making people seriously ill was now visible to all; and the increasing incidence was not going unnoticed. Secondly, on Friday 5 November 2004, the Secretary of State for Health, John Reid MP, in a landmark announcement stated '*I expect MRSA bloodstream infection rates to be halved in our hospitals by 2008*' (BBC, 2004). This was an IPCT '*where were you when... moment*'. Of note the ICNA Chairperson at the time was our very own Jean Laurence who was quoted on the BBC as saying '*To meet these expectations there will be a need to increase resources*' (BBC, 2004). It was more than increased resources we needed – it was a completely different strategy.

2006

In 2006, over 12 months after the Secretary of State's announcement and five years after the introduction of mandatory surveillance of MRSA bacteraemias, the new MRSA guidelines were published (Coia et al, 2006). Once again the same professional groups made up the working party and contributed to the revision of the twice-previously

revised guidance. The explicit task was 'to revise the guidelines with an enhanced focus on the prevention and control of MRSA infections in the UK' (Coia et al, 2006). This time the production process was open. The databases were used and the search questions were listed. The searches looked back to 1996, which meant that some of the rich vein of learning on *Staphylococcus aureus* in the 1960s and 1970s was neglected (Williams et al, 1960). Again acknowledging hindsight bias, it is now possible to determine that these questions were perhaps incomplete. The word 'infection' appears only once in the four questions asked: 'To what extent does environmental cleaning with detergent or detergent plus disinfectant contribute to the control of MRSA infection and what are the costs?' (Coia et al, 2006). The other questions related to screening of patients, surveillance and isolation or cohorting procedures. These remaining three questions all have the same tail, i.e. 'contribute to reducing the incidence of MRSA transmission.' Ergo, the searches looked for the efficacy of four interventions (surveillance, screening, isolation and cleaning or disinfection) and not specifically at how MRSA infections arise or how to prevent them. I would argue that preventing transmission and preventing infections are not synonymous. I also think it would have been helpful to have started with a discourse of the problem before examining the value of possible solutions, i.e. 'How does cross-transmission, and cross-infection, with MRSA (and or MSSA) arise in hospital environments?'

Within the 2006 guidelines, the authors cite work by Harbarth et al (2000) to illustrate the efficacy of controlling infection by controlling transmission:

'...MRSA bacteraemia correlates with hospital-wide prevalence and even delayed implementation of control measures had a substantial impact on both the reservoir of MRSA and the attack rate of MRSA bacteraemia' as quoted in Coia et al (2006).

The Harbarth et al (2000) paper, however, merits further scrutiny. MRSA-endemic hospitals in Geneva went from a zero additional precautions approach to what could be called a UK standard MRSA approach in 1993. They demonstrated substantial reductions in colonisations and infections. Four years after the introduction of control measures the Geneva hospitals were experiencing similar levels of MRSA to that experienced in the two years before their introduction (Harbarth et al, 2000). As the authors stated 'perhaps because there was a substantial delay in implementing control measures, total eradication was not possible' (Harbarth et al, 2000). This was a plausible explanation, but so was the explanation that controlling transmission will only get you so far – to prevent the remaining infections you need a concurrent strategy directed specifically at infection prevention. Harbarth et al (2000) showed that reducing colonisation reduced infection – but it did not eradicate the problem.

Also included in the 2006 guidance was an extensive section on antibiotic stewardship (Coia et al, 2006). Some of what had vexed earlier guideline writers, e.g. agency nurses and *S. aureus* dispersers received scant or no attention. The agency nurse statement was abridged to: 'The special difficulties and risks posed by agency and locum staff should be considered (Category 1b)' (Coia et al, 2006). However, the specifics of the considerations are limited and no active recommendations are made. The identification of dispersers deemed necessary in the 1986, 1990 and 1998 guidance was no longer included in the 2006 guidance (Anon, 1986, 1990, 1998; Coia et al, 2006). There were advantages to identifying MRSA at that time. Specifically there was a high degree of assurance that isolation of MRSA equated to evidence of nosocomial cross transmission. As a consequence its use as a marker of infection prevention and control was advocated and exploited in some areas (Curran et al, 2002).

The 2006 guidance was radical in its approach and dedicated an entire section to local surveillance. There was an embryonic approach to quality improvement included within the discussion with the illustration of statistical process control charts (SPCs) and a cause and effect chart (Coia et al, 2006). The SPC and cause and effect charts were mine, and I will be eternally grateful to the only mention of invasive devices in the entire document, which appears in the cause and effect chart 'Avoid use of invasive devices – remove any devices as soon as possible' (Coia et al, 2006). Of note however the overall aim in the cause and effect chart was minimising cross transmission. We were getting there but preventing infections was still subservient to preventing transmission. In the years since the publication of the 2006 guidance the embryonic quality improvement approach ultimately developed and has borne fruit (perhaps alongside a naturally declining MRSA (Wyllie et al, 2011; Curran, 2014)).

What would I do differently if faced with a similar emerging problem today?

Over the past 30 years, guidelines were produced to try and stop MRSA from establishing itself where it was not endemic, and trying to eradicate it where it was, using inadequate resources (surveillance, laboratory identification and environments). An examination of these MRSA guidelines (with acknowledged hindsight bias), has identified what I think needs further attention. This can be summed up as the guideline purpose, the expectations and the impact assessment. The purpose of the guidance (despite what titles said) was to prevent transmission when what was required with equal focus was the prevention of infection. Because expectations of success were so low, there was little to be gained (and much to be lost) by advocating draconian control measures. Also, as the advocated control measures were so extensive, an impact assessment should have been done concurrently to provide confirmation that these control measures were at least feasible.

Although the evidence for any particular control measure may be robust, e.g. closing a ward will stop transmission to patients who are not currently in the ward, for the healthcare system itself we will have cured the disease by killing the patient. It must be understood that it is the healthcare systems that (unintentionally) design-in cross transmission and cross infection and it is the healthcare systems that needs to adopt changes into their systems which will prevent cross transmission and infection. The guidance writers' goal therefore is to design-in IPC without significant impact on the healthcare system's purpose. To do this a wider literature than that produced by the IPC community is required, e.g. systems thinking and human factors sciences.

Writing guidelines has developed significantly from the early iterations discussed here. There are now accepted and accredited methodologies (Scottish Intercollegiate Guidelines Network, 2011). However, evidence-based guideline production for IPC will always be an imperfect art. This is because the IPC literature is itself imperfect; new or re-emerging organisms may not necessarily behave the same as genetically related organisms that have gone before. Ergo, control measures could be either in excess of, or insufficient, to gain control. For example, it was not until outbreaks of SARS arose, and the evidence on the modes of transmission was gathered, including the implications of super-spreaders, that control measures sufficient to gain control were introduced (Seto et al, 2003). Similarly, the MRSA from the 1980s onwards behaved differently to those that went before. It is accepted that data on new and emerging pathogens is often weak and sometimes nonexistent; nevertheless, as John Snow demonstrated, control measures can still be very effective (Hennekens and Buring, 1987).

What I would do differently (next time) is to better understand both the problem (i.e. continuous assessment of the infections and or/ colonisations being caused) and the healthcare systems that are generating the problem; this will identify system levers that can and

should be altered to reduce risks. The IPC community should continuously and proactively be recognising, assessing and advising on the outbreak-provoking factors that are present and being generated by those who design healthcare systems and by those who choose the indicators on which healthcare systems are adjudicated.

Summary

With hindsight bias the MRSA guidelines of the past have been critiqued; it is acknowledged that there are many unique challenges to the production of successful IPC guidelines.

Future IPC guidance – regardless of the organism – should be flexible and include feedback loops (local to national to local) to make sure that recommended control measures remain achievable and desirable throughout the lifetime of the guidance. Going forward, cross transmission and cross infection must be seen as healthcare system-generated outputs.

Local IPC surveillance systems should be recognised as the major defence mechanism mitigating against healthcare outbreaks (incidence and impact). Uniform local surveillance data, inclusive of infection status, which was not available in the past and is still not currently available, should be introduced to help defend healthcare systems against emerging pathogens; perhaps something for the IPS to ponder and rectify.

As we embark on the control of CPE, the IPC community must ensure that we are prepared to understand the emerging organisms in the context of evolving healthcare systems.

With CPEs it appears we are heading for a perfect storm. Despite improvements in our environments and our infection prevention our in-patients have never been so debilitated, the organisms challenging us have never been so resistant, and our ability to identify who is shedding these organisms has never been so limited.

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I have enormous respect and professional admiration for all those who considered and deliberated on the best possible way to keep patients safe against emerging MRSA. It is in the context of continuous improvement that I have written this critique.

Acknowledgement 2

This is the 13th consecutive Outbreak Column and before the 14th I will take a break to reflect on how the column should be continued. I acknowledge that I have not written about recent *S. aureus* outbreaks as promised at the end of Outbreak Column 12. With the editor's permission I hope to do this as part of Outbreak Column 14.

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