Article:
Wilcox, MH orcid.org/0000-0002-4565-2868 (2017) The start of another infection prevention learning curve: reducing healthcare-associated Gram-negative bloodstream infections. Journal of Hospital Infection, 97 (3). pp. 205-206. ISSN 0195-6701

https://doi.org/10.1016/j.jhin.2017.10.004

The start of another infection prevention learning curve: reducing healthcare associated Gram-negative blood stream infections

Mark H. Wilcox

Consultant / Head of Microbiology Research and Development, Leeds Teaching Hospitals NHS Trust;

Professor of Medical Microbiology & Sir Edward Brotherton Chair of Bacteriology, University of Leeds;

Lead on *C. difficile* infection, Public Health England;

Medical Advisor to National Infection Prevention & Control Lead, NHS Improvement.

Corresponding author:

Professor Mark H. Wilcox

Microbiology,
Old Medical School,
Leeds General Infirmary,
Leeds LS1 3EX,
W. Yorks., UK.

mark.wilcox@nhs.net

Tel +44 113 392 6818
Fax +44 113 392 2696

A decade ago, many believed that reducing methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections (BSIs) by 50% was unachievable; in England the total declined by ~90% from its peak.[1] Similar incredulity surrounded a target in England to decrease *Clostridium difficile* infections by 30%, and yet today these number ~75% fewer.[1] These stark improvements are contrasted by an inexorable rise in Gram-negative (GN) BSIs; since 2012-13, *Escherichia coli* BSIs have increased by ~25% in England (from ~32,000 to ~41,000 in 2016-17), and so now dwarf MRSA BSIs at their peak by a ratio of about 5:1, and today by almost 50:1.[1] The increasing incidence of *E. coli* BSI is an international phenomenon. Between 2005-14 in a stable cohort of 32 hospitals in central France, the incidences of *E. coli* BSI more than doubled for community-acquired (CA) cases aged >75 years, CA-BSIs of digestive origin in patients aged 60-74 years, HA BSIs, and BSIs associated with extended-spectrum B-lactamase-producing strains.[2] Also, national surveillance data from Switzerland show significant increases in the incidence of BSIs caused by *E. coli*, and non-*E. coli Enterobacteriaceae* ($p<0.001$) between 2008-14.[3] Hence, the scale of the new National Health Service (NHS) ambition to reduce healthcare-associated (HA) GNBSIs by 50% by 2021 in England is daunting.[4]

So, where do we start? Firstly by looking backwards. Improvements in infection prevention practice, and antibiotic prescribing changes, helped achieve large reductions in MRSA BSI and CDI incidences, but have not stemmed the tide of GNBSIs.[5,6] This means that more of the same will not be sufficient. However, as previously demonstrated, the NHS is particularly well placed to deliver multi-modal infection prevention programmes that will be needed if we are to succeed with the HA GNBSI ambition. Notably, risk factor data and information on which interventions were/were not effective in the MRSA and CDI reduction era were not systematically recorded at a national level. It will be important to maximise the value of risk factor data collected via the Public Health England's Data Capture System. Indeed, this system will identify according to the data submitted which GN BSIs are HA, according to pre-set criteria.[4] In addition, the increased access to antibiotic prescribing and resistance data provide more opportunities to compare practice and potential risk factors for the selection of BSI pathogens.[7]

Of note, Gram-negative bacilli are endogenous potential pathogens and there is not good evidence to support cross-infection as a major contribution to HA GNBSIs. It is reasonable

to assume that maintenance of the current standards of infection prevention practice will limit the risk of cross-infection by enterobacteriaceae, although targeted improvements here could still be beneficial. So, interventions should attempt to reduce the risk of translocation and/or the selection of these bacteria. The continuing drive to eliminate unnecessary antibiotic prescribing could be beneficial here. Antibiotic exposure can have profound effects on the composition of the gut microbiome; frequently this is associated with reduced diversity and expansion of proteobacteria, including *E. coli* and related GN bacilli.[8] Such antibiotic-induced selection pressure could theoretically predispose to BSI, either via translocation of bacteria from the gut to blood, or indirectly by increased risk of contamination of skin or devices (e.g. urinary catheters). Thus, eliminating unjustified antibiotic administration, including overlong courses remains a worthwhile goal.

Enhanced surveillance of over 1700 *E. coli* BSIs in 35 hospitals across England showed, as expected, that the urogenital tract was the most frequently reported source of infection (51.2% of cases).[9] Prior urinary tract infection treatment was the largest risk factor associated with this source. Previous healthcare exposure within one month occurred in half of the patients; between one third and one fifth of these had antimicrobial therapy or urinary catheterization. Such observational data suggest that optimising urinary catheter care (including using this only when clearly required and for as short a duration as possible), and improved antibiotic management of urinary tract infections should be targeted initially. The next most common 'sources' of *E. coli* BSI were considered to be hepatobiliary, gastrointestinal and neutropenia. Thus, on a pure numbers basis, it makes sense to target the above index diseases to make the greatest inroads to reducing HA GNBSIs.

In the above surveillance study more than two-thirds of patients had a positive blood culture taken by 1 day after admission.[9] This fact strongly endorses the need for a whole health economy approach to reducing (even HA) GN BSIs. Cases should be reviewed locally to determine what are the most common sources of infection. Interventions should initially focus on ensuring that recommended management pathways are being followed optimally, especially in the index diseases outlined above. Local intervention plans should be tailored initially from the available best practice infection prevention bundles. It will be important to keep good records about interventions, especially evidence on the extent of compliance

with guidelines and local plans. Such carefully assessed data will be needed to identify potential new intervention strategies that can then be further explored across the NHS.

HA GN BSIs are a healthcare safety issue. They are associated with excess morbidity, mortality and hospital length of stay.[10] We should not accept the continuing increasing incidence of these infections as an inevitability. It is plausible that concerted practice changes could be effective in reducing HA GNBSIs in England. Whilst this is undoubtedly a major challenge, are the prospects of success really less realistic than the targets that were met and surpassed for MRSA and CDI?

Funding

None

Conflicts of interest

None

References

1. Public Health England. Healthcare associated infections (HCAI): guidance, data and analysis. Available at: https://www.gov.uk/government/collections/healthcare-associated-infections-hcai-guidance-data-and-analysis Last accessed 07 October 2017.
2. van der Mee-Marquet NL, Blanc DS, Gbaguidi-Haore H *et al*. Marked increase in incidence for bloodstream infections due to Escherichia coli, a side effect of previous antibiotic therapy in the elderly. Front Microbiol 2015;6:646.
3. Buetti N, Atkinson A, Marschall J, Kronenberg A; Swiss Centre for Antibiotic Resistance (ANRESIS). Incidence of bloodstream infections: a nationwide surveillance of acute care hospitals in Switzerland 2008-2014. BMJ Open 2017;7(3):e013665.
4. NHS Improvement. Preventing healthcare associated Gram-negative bacterial bloodstream infections. Available at:

https://improvement.nhs.uk/resources/preventing-gram-negative-bloodstream-infections/ Last accessed 07 October 2017.

5. Duerden BI, Johnson A, Fry C, Wilcox MH. The control of meticillin-resistant *Staphylococcus aureus* (MRSA) blood stream infections in England. Open Forum Infectious Diseases 2015;2:ofv035.
6. Dingle KE, Didelot XD, Quan TP, Eyre DW, Stoesser N, Golubchik T, Harding RM, Wilson DJ, Griffiths D, Vaughan A, Finney JM, Wyllie DH, Oakley SJ, the Modernising Medical Microbiology Informatics Group, Fawley WN, Freeman J, Morris K, Martin J, Howard P, Gorbach S, Goldstein EJC, Citron DM, Hopkins S, Hope R, Johnson AP, Wilcox MH, Peto TEA, Walker AS, Crook DW; Modernising Medical Microbiology Informatics Group. Effects of control interventions on Clostridium difficile infection in England: an observational study. Lancet Infect Dis 2017;17:411-421.
7. Public Health England. AMR local indicators. Available at: https://fingertips.phe.org.uk/profile/amr-local-indicators Last accessed 07 October 2017.
8. Hill DA, Hoffmann C, Abt MC, Du Y, Kobuley D, Kirn TJ, Bushman FD, Artis D. Metagenomic analyses reveal antibiotic-induced temporal and spatial changes in intestinal microbiota with associated alterations in immune cell homeostasis. Mucosal Immunol 2010;3:148-58.
9. Abernethy J, Guy R, Sheridan E, Hopkins S, Kiernan M, Wilcox M, Johnson J, Hope R, on behalf of the E. coli bacteraemia sentinel surveillance group. Epidemiology of Escherichia coli bacteraemia in England: results of an enhanced sentinel surveillance programme. J Hosp Infect 2017;95:365-75.
10. Naylor NR, Pouwels KB, Hope R, Green N, Henderson KL, Knight GM, Atun R, Robotham JV, Deeny S. A National Estimate of the Health and Cost Burden of *Escherichia coli* Bacteraemia in the Hospital Setting: The Importance of Antibiotic Resistance. bioRxiv 2017. doi: https://doi.org/10.1101/153775