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Editorial

Antimicrobial stewardship in the post COVID-19 pandemic era: an opportunity for renewed focus on controlling the threat of antimicrobial resistance

In 2015, the World Health Organization (WHO), World Health Assembly adopted a global action plan on antimicrobial resistance involving 5 main objectives which included: raising public and provider awareness, investment in diagnostics and therapeutics, improving surveillance systems, prevention of infections, and optimising the use of antimicrobials [1]. However, during the COVID-19 pandemic period, wider attention to antimicrobial stewardship (AMS), and its impact on general antimicrobial resistance (AMR) has reduced [2]. Equally important is the fact that whilst these strategies were announced in 2015 by the WHO, the focus on antimicrobial resistance, had not been sustained, even before the pandemic [3]. As we emerge from this pandemic, the WHO World Antimicrobial Awareness Week (WAAW), offers an opportunity to reflect on the lessons learnt from the events of the last two years, in order to re-energise and re-focus attention on the global burden of antimicrobial resistance. WAAW is globally celebrated from 18 to 24 November every year; in recognition, the Journal of Hospital Infection is publishing a special section focused on AMR and AMS.

Globally, the consumption of antibiotics increased by 65% between 2000 and 2015, with an increase of daily defined doses per 1000 people from 11.3 to 15.7 [4]. This rise has led to concerns of potential increases in AMR and the WHO has classified antibiotics into three main categories: Access (narrowest spectrum, with reduced potential for resistance; these should be widely available, accounting for 60% of antibiotic consumption), Watch (specifically indicated for limited syndromes, with resistance more likely) and Reserve (last resort antibiotics) [5]. However, an early implementation study from WHO showed that in some countries Watch category antibiotics accounted for over 50% of antibiotics utilised [5]. Hence, although the AMS strategy needs to be global, approaches should be adapted to local practices, ensuring access to important therapeutic agents whilst preserving their long term availability [6–9]. However, challenges remain on a global scale, with a rising population and antibiotic consumption projected to increase worldwide by 200% between 2015 and 2030 [4].

The early phases of the COVID-19 pandemic produced new challenges in diagnostics and use of antimicrobials due to significant numbers of patients being admitted with a novel respiratory disease. In the absence of objective evidence, physicians often used antibiotics based on experience with bacterial superinfection in Influenza [10]. However, with time, evidence has grown to support AMS in patients with COVID-19. Data now shows that serum markers can be used to withhold broad-spectrum antibiotics in patients with COVID-19 [11]. Additionally, Chan *et al.* demonstrated that re-implementation of multi-disciplinary ward rounds involving pharmacists and microbiologists, following the first COVID-19 wave, led to a reduction in the use of broad-spectrum antimicrobial agents with no change in overall mortality in intensive care patients [12]. In this issue, Ali *et al.*, publish an audit, highlighting the importance of reviewing antimicrobial treatments following diagnostic tests, where COVID-19 was part of the working diagnoses, to optimise treatments in line with the "Start Smart, Then Focus" approach [13].

Fungal infections have also played a significant role in patients with COVID-19, due to the usage of immunosuppressing therapies [14–17]. In this context, the use of antifungals has increased at a time when there is increasing recognition of the emerging threat of antifungal resistance [18] The publication by O'Shea *et al.*, is therefore timely, because it offers a practical and pragmatic solution through a fungal diagnostic algorithm for antifungal stewardship in patients with COVID-19 infection [19]. Furthermore, it has also been well documented that the COVID-19 pandemic caused an increase in incidence of hospital onset bloodstream infections, particularly of Gram negative aetiology [20]. Torrecillas *et al.* reported not only an increased incidence of Gram negative bloodstream infection in ventilated patients during the pandemic, but also an increase in consumption of broader spectrum antimicrobials [21].

Moving forward, the impact on healthcare systems worldwide that rapidly re-organised to cope with the COVID-19 pandemic are becoming increasingly apparent. Large numbers of patients are now waiting for surgical procedures and there will inevitably be a drive to reduce waiting lists [22]. Assessing the need for antibiotic prophylaxis, linked to rates of healthcare acquired infection, will be critical. Reidy *et al.* concisely demonstrated that local surveillance can support scientific evidence and international guidance, by showing that antimicrobial prophylaxis is not beneficial in preventing catheter related bacteraemia following central venous catheter insertion [23].

Furthermore, monitoring the organisms and associated resistance profiles from these infections will become increasingly relevant, to prevent collateral damage from AMR arising from increased surgical prophylaxis [24]. It is clear that more work remains because, Morioka *et al.* demonstrate a significant variation in relation to adherence to surgical antimicrobial prophylaxis prescribing in 16 hospitals encompassing 18 types

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of surgery; ranging from 8% to 92%, with an overall adherence of 47% [25]. AMS is not only about adherence to guidelines, but also about ensuring the agents recommended for prophylaxis in guidelines are appropriate for the causative organisms of infection. In this issue Widmer *et al.*, challenge the current recommendations of cephalosporin prophylaxis for patients undergoing trans-catheter aortic valve replacement (TAVR), demonstrating the presence of Enterococci at the site of vascular access even after skin disinfection. [26] Enterococci are recognised to be the commonest cause of post-TAVR infective endocarditis, but more studies are needed to understand whether infection is occurring at the time of valve insertion through persistent groin colonisation. [26,27] Optimising the use of antimicrobials in all settings remains a goal in AMS, with Chow *et al.* reporting on a study focusing on better understanding the uptake and usage of an antibiotic guideline app by physicians [28]. The study showed that while the usefulness of the app was important, a strong social influence was the primary determiner for usage, highlighting that social networks within healthcare organisations can increase the uptake of clinical decision tools such as mobile phone applications [28].

Raising both public and healthcare provider awareness and knowledge remains an important component for reducing AMR within the WHO Global action plan [1]. Within AMS and antimicrobial stewardship programmes, education is a vital strategy and there is evidence that it positively impacts prescribing behaviours [29]. However, there have been few studies assessing education towards other healthcare providers, such as pharmacists, nurses, or even other members of the stewardship team [29]. In this issue of the JHI, we publish two studies focusing on antimicrobial stewardship within nursing teams. Chater *et al.*, performed a cross-sectional multi-country survey focusing the determinants of nurse AMS behaviours [30]. The study showed that nurses with AMS training performed significantly higher in all nine behaviours studied, including use of infection control precautions, monitoring patients for side-effects of antimicrobials, and initiating the switch from intravenous to oral antimicrobials [30]. Ju *et al.* also publish in this issue; a study from South Korea involving 1160 nurse participants, they demonstrate that most respondents agreed that a strong knowledge of antimicrobials and AMS was necessary, but hospitals needed to provide AMS and AMR training through national-level approaches [31].

Prevention of infections is a further component of the WHO global action plan which is achieved through interventions such as vaccination, good infection prevention and control policies, and sanitation [1]. It is through these interventions involving infection prevention and control (IPC) that antimicrobial consumption can be further reduced both in the community and hospitals, through reducing rates of infection. Examples where such interventions have been effective at reducing antimicrobials include those implementing bundles for lowering surgical site infection [32,33]. Additionally in this issue, Umemura *et al.* demonstrate that cleaning with a chlorine-based agent and implementation of an AMS programme led to a reduction in hospital-onset Clostridioides difficile infection. This shows that the hospital environment (infection prevention and control), and antimicrobial stewardship have an impact on healthcare associated infections. Hence there is increasing recognition that both AMS and infection prevention and control are inter-dependent; and they need to closely interlink in order to control AMR within healthcare settings [34].

Prior to the COVID-19 pandemic, there was considerable focus on AMS as a route to reducing AMR. IPC at the time was considered by many to be a challenge where solutions were largely available and well researched. The COVID-19 pandemic has proven that IPC within hospitals, primary care settings and the wider community remains an ongoing challenge, through aspects such as building ventilation, patient pathways, isolation facilities and diagnostic strategies. During the pandemic, AMS has largely become a problem to be addressed in the future. Yet the threat of AMR remains and continues to grow. As we move into the post-pandemic era, it is time to establish a new paradigm for the control and reduction of AMR, where IPC and AMS are considered "two sides of the same coin". It is only through collaboration between specialists in IPC and leaders in antimicrobial stewardship that we will be able to tackle the far greater challenge of global antimicrobial resistance.

Conflict of interest statement

Nikunj Mahida, Martyn Wilkinson and Jim Gray are editors at the Journal of Hospital Infection.

Gemma Winzor and Pauline Jumaa are editors at Infection Prevention in Practice.

References

[1] WHO. Global action plan on antimicrobial resistance. 2015. http://www.who.int/drugresistance/global_action_plan/en/. [Accessed 14 August 2022].

[2] Lynch C, Mahida N, Gray J. Antimicrobial stewardship: a COVID casualty? J Hosp Infect 2020;206:401–3. https://doi.org/10.1016/j.jhin.2020.10.002.

[3] Laxminarayan R, Van Boeckel T, Frost I, Kariuki S, Khan EA, Limmathurotsakul D, et al. The Lancet infectious diseases Commission on antimicrobial resistance: 6 years later. Lancet Infect Dis 2020;20:e51–60. https://doi.org/10.1016/S1473-3099(20)30003-7.

[4] Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc Natl Acad Sci USA 2018;115:e3463–70. https://doi.org/10.1073/pnas.1717295115.

[5] Work Health Organisation. WHO report on surveillance of antibiotic consumption. 2018. https://apps.who.int/iris/handle/10665/277359. [Accessed 14 August 2022].

[6] Siachalinga L, Mufwambi W, Lee LH. Impact of Antimicrobial Stewardship Interventions to Improve Antibiotic Prescribing for Hospital Inpatients in Africa: A Systematic Review and Meta-analysis. J Hosp Infect 2022. https://doi.org/10.1016/j.jhin.2022.07.031. S0195-6701(22)00253-5.

[7] Nguyen HQ, Nguyen-Thi HY, Huynh PT, Le NDT, Nguyen NT, Hsia Y. Effectiveness of an enhanced antibiotic stewardship programme among paediatric patients in a tertiary hospital in Vietnam. J Hosp Infect 2022;127:121–8. https://doi.org/10.1016/j.jhin.2022.06.002.

[8] Renggli L, Gasser M, Plüss-Suard C, Kronenberg A. Consumption of anti-meticillin-resistant Staphylococcus aureus antibiotics in Swiss hospitals is associated with antibiotic stewardship measures. J Hosp Infect 2021;117:165–71. https://doi.org/10.1016/j.jhin.2021.08.019.

[9] Paz V, D'Agostino ML, Garibaldi F, Orellana R, Paniagua M, Santillán A. Multiplex PCR in the empirical antibiotic treatment of patients with SARS-CoV-2 and bacterial respiratory superinfection. Infection Prevention in Practice 2022;4(3):100227. https://doi.org/10.1016/j.infpip.2022.100227.

[10] Huttner BD, Catho G, Pano-Pardo JR, Pulcini C, Schouten J. COVID-19: don't neglect antimicrobial stewardship principles. Clin Microbiol Infect 2020;26:808—10. https://doi.org/10.1016/j.cmi.2020.04.024.

[11] Williams EJ, Mair L, Silva TI de, Green DJ, House P, Cawthron K, et al. Evaluation of procalcitonin as a contribution to antimicrobial stewardship in SARS-CoV-2 infection: a retrospective cohort study. J Hosp Infect 2021;110:103—7. https://doi.org/10.1016/j.jhin.2021.01.006.

[12] Chan XHS, O'Connor CJ, Martyn E, Clegg AJ, Choy BJK, Soares AL, et al. Comparison of antibiotic use between the first two waves of COVID-19 in an Intensive Care Unit at a London Tertiary Centre: reducing broad-spectrum antimicrobial use did not adversely affect mortality. J Hosp Infect 2022;124:37—46.

[13] Ali S, Williams R, Canavan J, Hickey C, Doyle M. An Audit on Adherence to Antimicrobial Prescribing Guidelines during Wave One of the SARS-CoV-2 Pandemic. J Hosp Infect 2022 Jul 10. https://doi.org/10.1016/j.jhin.2022.06.019. S0195-6701(22)00225-0.

[14] Rawson TM, Moore LSP, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, et al. Bacterial and Fungal Coinfection in Individuals With Coronavirus: A Rapid Review To Support COVID-19 Antimicrobial Prescribing. Clin Infect Dis 2020;71:2459—68. https://doi.org/10.1093/cid/ciaa530.

[15] Minihan B, McAuliffe E, Powell J, Wong SL, Wilkie K, Murphy C, et al. Association between tocilizumab treatment of hyperinflammatory patients with COVID-19 in a critical care setting and elevated incidence of hospital-acquired bacterial and invasive fungal infections. J Hosp Infect 2022;126:29—36. https://doi.org/10.1016/j.jhin.2022.04.007.

[16] Chong WH, Neu KP. Incidence, diagnosis and outcomes of COVID-19-associated pulmonary aspergillosis (CAPA): a systematic review. J Hosp Infect 2021;113:115—29. https://doi.org/10.1016/j.jhin.2021.04.012.

[17] Silva DL, Lima CM, Magalhães VCR, Baltazar LM, Peres NTA, Caligiorne RB, et al. Fungal and bacterial coinfections increase mortality of severely ill COVID-19 patients. J Hosp Infect 2021;113:145—54. https://doi.org/10.1016/j.jhin.2021.04.001.

[18] Fisher MC, Alastruey-Izquierdo A, Berman J, Bicanic T, Bignell EM, Bowyer P, et al. Tackling the emerging threat of antifungal resistance to human health. Nat Rev Microbiol 2022;20:557—71. https://doi.org/10.1038/s41579-022-00720-1.

[19] O'Shea M, Birkhamshaw E, Khalil R, Wickramasinghe N, Hamad M, Crooks N, et al. Implementation of a diagnostic algorithm for COVID-19-associated Pulmonary Aspergillosis. J Hosp Infect 2022. https://doi.org/10.1016/j.jhin.2022.07.023. S0195-6701(22)00240-7.

[20] Sloot R, Nsonwu O, Chudasama D, Rooney G, Pearson C, Choi H, et al. Rising rates of hospital-onset Klebsiella spp. and pseudomonas aeruginosa bacteraemia in NHS acute trusts in England: a review of national surveillance data, August 2020-February 2021. J Hosp Infect 2022;119:175—81. https://doi.org/10.1016/j.jhin.2021.08.027.

[21] Torrecillas M, Gumucio VD, Padullés A, Tubau F, Marco D, Shaw E, et al. Antimicrobial use and aetiology of bloodstream infections in critically ill patients during early stages of SARS-CoV-2 pandemic. Infection Prevention in Practice 2022:100241. https://doi.org/10.1016/j.infpip.2022.100241.

[22] The Lancet Rheumatology. Too long to wait: the impact of COVID-19 on elective surgery. Lancet Rheumatol 2021 Feb;3(2):e83. https://doi.org/10.1016/S2665-9913(21)00001-1.

[23] Reidy N, Moore D, Mulrooney C, Abdalrahaman S, Chan G, McWade R, et al. Antimicrobial prophylaxis for dialysis catheter insertion: Does the infection data support it? Infect Prev Pract 2022;4:100204. https://doi.org/10.1016/j.infpip.2022.100204.

[24] Schreiber PW, Laager M, Boggian K, Neofytos D, van Delden C, Egli A, et al. Surgical site infections after simultaneous pancreas kidney and pancreas transplantation in the Swiss Transplant Cohort Study. J Hosp Infect 2022. https://doi.org/10.1016/j.jhin.2022.07.009. S0195-6701(22)00224-00229.

[25] Morioka H, Ohge H, Nagao M, Kato H, Kokado R, Yamada K, et al. Appropriateness of surgical antimicrobial prophylaxis in Japanese university hospitals. J Hosp Infect 2022 Jul 11. https://doi.org/10.1016/j.jhin.2022.06.017. S0195-6701(22)00218-3.

[26] Widmer D, Widmer AF, Jeger R, Dangel M, Stortecky S, Frei R, et al. Prevalence of enterococcal groin colonization in patients undergoing cardiac interventions: Challenging antimicrobial prophylaxis with cephalosporins in TAVR patients. J Hosp Infect 2022. https://doi.org/10.1016/j.jhin.2022.07.020. S0195-6701(22)00242-0.

[27] Khan A, Aslam A, Satti KN, Ashiq S. Infective endocarditis post-transcatheter aortic valve implantation (TAVI), microbiological profile and clinical outcomes: A systematic review. PLoS One 2020;15:e0225077. https://doi.org/10.1371/journal.pone.0225077.

[28] Chow A, Huang Z, Yeow A, Lee J. Social influence is the main driver of emergency physicians' intention to use an antibiotic clinical decision support mobile application. J Hosp Infect 2022. https://doi.org/10.1016/j.jhin.2022.07.018. S0195-6701(22)00239-0.

[29] Satterfield J, Miesner AR, Percival KM. The role of education in antimicrobial stewardship. J Hosp Infect 2020;105:130—41. https://doi.org/10.1016/j.jhin.2020.03.028.

[30] Chater AM, Family H, Abraao LM, Burnett E, Castro-Sanchez E, Du Toit B, et al. Influences on nurses' engagement in antimicrobial stewardship behaviours: A multi-country survey using the Theoretical Domains Framework. J Hosp Infect 2022. https://doi.org/10.1016/j.jhin.2022.07.010. S0195-6701(22)227-4.

[31] Ju J, Han K, Ryu J, Cho H. Nurses' attitudes toward antimicrobial stewardship in South Korea. J Hosp Infect 2022. https://doi.org/10.1016/j.jhin.2022.07.016. S0195-6701(22)00237-7.

[32] Dixon LK, Biggs S, Messenger D, Shabbir J. Surgical site infection prevention bundle in elective colorectal surgery. J Hosp Infect 2022;122:162—7. https://doi.org/10.1016/j.jhin.2022.01.023.

[33] Locke T, Parsons H, Briffa N, Stott M, de Silva TI, Darton TC. A bundle of infection control measures reduces postoperative sternal wound infection due to Staphylococcus aureus but not Gram-negative bacteria: a retrospective analysis of 6903 patient episodes. J Hosp Infect 2022;126:21—8. https://doi.org/10.1016/j.jhin.2022.03.006.

[34] Wade T, Heneghan C, Roberts N, Curtis D, Williams V, Onakpoya I. Healthcare-associated infections and the prescribing of antibiotics in hospitalized patients of the Caribbean Community (CARICOM) states: a mixed-methods systematic review. J Hosp Infect 2021;110:122—32. https://doi.org/10.1016/j.jhin.2021.01.012.

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