Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Protecting intubated patients from the threat of antimicrobial resistant infections with monoclonal antibodies

Recognition that immunisation might affect antimicrobial resistance is increasing. Many traditional bacterial vaccines continue to be effective, without the generation and expansion of bacterial escapee subpopulations, suggesting that vaccines deployed to control antimicrobial resistant bacteria are likely to be effective for substantially longer than are novel antimicrobials.[1,2] The WHO list for antimicrobial resistance priority pathogens contains several bacteria for which there are no licensed vaccines or any vaccine development activity by big pharmaceutical companies (appendix p 1).[3,4] Among these pathogens, carbapenem-resistant *Acinetobacter baumannii* is treatable only with colistin (ie, a last-resort antimicrobial) and, with 8500 cases and 700 associated deaths in the USA in 2017, has been identified as an urgent threat by the US Center for Disease Control and Prevention.[5] This pathogen is also widespread in Europe; as of 2018, more than 50% of the *A baumannii* isolated in Italy, Greece, Croatia, and Poland were carbapenem resistant and treatable only with colistin.[6]

The presence of carbapenem-resistant *A baumannii* in a hospital setting, particularly within intensive care units (ICUs), in which it affects patients who are intubated for mechanical ventilation, is a major concern. A year-long study in 2018 of 12 tertiary care hospitals in Italy identified 281 cases of carbapenem-resistant *A baumannii* bloodstream infections; this case series had a 30 day mortality of 74% (207 of 281).[7] The issue is worse in many low-income and middle-income countries, in which poor health-care facilities, unlegislated antimicrobial usage, and large populations further compound the problem. COVID-19 has been a tragedy for human health. The potential for an increased number of people who require intubation in ICUs because of COVID-19, and are at possible risk of carbapenem-resistant *A baumannii* and other bacterial infections related to antimicrobial resistance, is truly terrifying and has not been addressed. An ignorance of repeated warning signs, alongside minimal concerted preparedness to mitigate the effects of a respiratory virus pandemic, are reflected in this situation with antimicrobial resistance.

Could the use of bacterial vaccines address this scenario? Clearly vaccines could play a role, but there are two major caveats. First, vaccines are given prophylactically and require time postimmunisation for individuals to develop protective immunity. Second, people who are admitted to ICUs typically have underlying comorbidities, resulting in immunosuppression. Therefore, even if they have been vaccinated on admission to an ICU, they are unlikely to mount an adequate immune response to prevent a serious infection. The same argument could be applied to almost all major bacterial infections that are associated with health-care settings.

See Online for appendix

Monoclonal antibody therapy could instantly provide the immunity that is normally afforded by vaccination and has shown the ability to significantly affect clinical bacterial infections. Bezlotoxumab is a licensed monoclonal antibody that reduces the possibility of the recurrence of *Clostridioides difficile* when administered with standard of care antimicrobials during a primary infection in a health-care setting.[8] Monoclonal antibodies are especially advantageous in this context in that, by working as an adjunct to standard of care, they could potentially extend antimicrobial shelf-life by killing surviving bacteria as resistance develops. An analysis of the preclinical pipelines for antimicrobials now shows a substantial number of monoclonal antibody programmes for infectious disease, suggesting a growing interest in monoclonal antibodies as a genuine alternative for small molecules in future clinical trials.[9]

Targeted deployment of monoclonal antibody therapies for specific pathogens related to antimicrobial resistance is likely to save lives and consequently reduce the duration of stays in ICUs, which in turn decreases the associated health-care costs. Any bacterial antigen can be targeted, protein or carbohydrate, and multiple platforms can be exploited to identify monoclonal antibodies, including phage-based screening assays, transgenic mice with a human immune repertoire, and B-cell repertoires from convalescent patients. These approaches will substantially widen the range of potential targets for monoclonal antibodies, hypothetically resulting in novel treatments that can work alongside current approaches.

The need to address antimicrobial resistance goes far beyond the treatment of intubated patients who are vulnerable in ICUs. The global threat posed by antimicrobial resistance will not disappear in our lifetime and the impasse between the clear need for new therapeutic approaches for drug-resistant bacterial infections and the scarce interest of pharmaceutical companies in delivering these novel therapeutics should be overcome with a degree of urgency. The engagement of cutting edge science provides versatile platforms for both single B-cell and pathogen genomics and high-throughput screening approaches to evaluate monoclonal antibody binding to known and unknown molecular targets. For target identification, the use of versatile platforms could potentially lead to new therapeutic opportunities that can be tested for proof of concept. Although the technology might be available, the impetus is scarce. The provision of an armoury of effective monoclonal antibodies from which to develop new therapies could be essential to stop the increasing number of bacterial pathogens that are antimicrobial resistant.

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