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Guest Editorial

Meningococcal Disease

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Polysaccharide encapsulated bacteria, including *Streptococcus pneumoniae, Haemophilus influenzae* type b (Hib), *Neisseria meningitidis,* Group B Streptococci, and *Salmonella* Typhi drive the use, and over-use of antibiotics globally. Most doctors don't prescribe antibiotics for viral infections, they prescribe them in case it is one of these bacteria that is causing the clinical symptoms displayed in the patient before them, leading to inappropriate antibiotic treatment of viral infections, and contributing to the rise in antimicrobial resistance (AMR). It is not surprising, indeed it is logical, that clinicians should treat these serious bacterial infections with antibiotics since they all have high morbidity and mortality associated with them. The problem of antibiotic over-use is even greater in countries where antibiotics are readily available over the counter and it is left to parents to decide whether a febrile illness should be treated with antibiotics, or not. Even in the most sophisticated settings, it is difficult for a doctor to separate occasional early serious sepsis from the avalanche of viral infections that present to clinical care. We now have access to licensed vaccines that can prevent many of these infections, and can be used to curb antibiotic overuse, but early recognition and rapid diagnostics will be needed for the cases that cannot be prevented.

Of these infections, meningococcal disease is the one which is most feared by the public in the United Kingdom. However, the successful awareness campaigns led by the meningitis charities and vivid images of the disease and its complications shown in the media have led to concern about this disease being prominent among the fears of parents and frontline doctors (**see Section 4 in this issue**). The concerns about this disease are legitimate given the rapid onset of illness among those affected and the high mortality, especially among those with septicaemia, but the probability of infection is very low for any individual child. Despite the low attack rate, meningococcal disease has been consistently the leading infectious cause of death among young children over the past decade.

Diagnostic tests that could determine who does not have a serious bacterial infection (and therefore who does not need antibiotics) could simplify management and reduce antibiotic use and risk of non-treatment. Unfortunately, such a diagnostic does not yet exist for management of febrile children. Indeed, while it seems increasingly possible to develop a better rule-in test, which points to a high likelihood of bacterial infection, a more useful rule-out test to identify those who don't need antibiotics, remains stubbornly elusive. For the rule-in test, promising approaches include molecular pathogen-specific tests, such as those described in **Section 3** for meningococcus, which are exquisitely sensitive and can be useful, unlike bacterial culture, even in the context of prior antibiotic treatment. Clinical decision rules have been widely used in clinical studies and usually include some routine laboratory tests to support decision-making and a new promising approach using RNA sequencing has recently been described[1]. However, none have yet been validated as safe rule-out tests and clinicians are still stuck with the antibiotic dilemma in managing patients.

For patients with serious rare diseases, like meningococcal disease, when it is recognised, it is of great importance that doctors have clear guidelines about optimal management. It has become clear that the optimising the early hours of management can improve outcomes[2]. In **Section 3** approaches to management are outlined, as are excellent resources to aid initial treatment.

Perhaps the optimal solution to tackle the problem of AMR is the use of vaccines, which lead to avoidance of antimicrobial use by preventing the infection in the first place. Hib vaccine, introduced in the UK in 1992 has virtually eliminated Hib and the 1999 introduction of a vaccine against capsular group C *Neisseria meningitidis* (MenC) has had a similar and sustained impact on that disease too (**see Section 2**). Pneumococcal infections in children are also down since the introduction of pneumococcal conjugate vaccines (PCV) in 2006[3]. The MenC vaccine was introduced to control a clonal outbreak of disease during the 1990s, but other capsular groups continued to circulate and cause disease. From 2011 a new outbreak caused by a capsular group W strain, spread to the UK from Latin America[4], and the response was the urgent introduction of a meningococcal vaccine covering capsular groups A, C, Y and W for adolescents in 2015 which will likely control this outbreak once sufficient cohorts have been vaccinated[4]. The commencement of a programme for MenB in 2015 makes the UK the only country in the world to be attempting control of disease caused by all of the major disease-causing capsular groups of meningococcus[5,6].

Unfortunately, not all bacterial infection is preventable at present. New vaccines for Group B Streptococcus are on the horizon, and could be an important step forward in reducing the morbidity and mortality associated with neonatal infection and are likely to be widely deployed.

While, these vaccine programmes, discussed above, are directly driving reductions in disease in the UK caused by polysaccharide encapsulated bacteria (**discussed in Section**

2)[7], vaccine programmes which prevent viral infections may also be important in the prevention of bacterial infections, since the latter may be complications of viral illnesses. For example, influenza has been associated with pneumococcal pneumonia and meningococcal disease, varicella with Group A streptococcal infection. Efforts to develop a respiratory syncytial virus (RSV) vaccine may eventually result in reductions in bacterial complications of viral lower respiratory tract infection (LRTI) in infants. Importantly, vaccines that prevent viral infections, such as influenza, will also reduce use inappropriate use of antimicrobials.

In the context of these vaccination programmes, that now allow policymakers to target all of the main bacterial causes of acute serious sepsis in children in developed countries (with the exception of (GBS) in the neonate), it is very difficult for young clinicians to become experienced in the management of severe sepsis. The problem of identifying the "needle in the growing haystack" of bacterial sepsis among the flood of viral infections is ever more challenging. The work of the meningitis charities (**section 4**) and the sepsis campaign has led to the development of tools to improve education of doctors about the symptom of severe bacterial infection.

We can be optimistic about further reductions in meningococcal disease and other serious bacterial infections, and their complications, in the UK, because we have such a comprehensive programme, which is still expanding to new cohorts. Vaccine programmes have undoubtedly had a huge impact on disease rates and associated mortality/morbidity and the improved focus on treatment guidelines and education about sepsis should better prepare the future clinical work-force for tackling the disease, and reducing inappropriate antibiotic usage.

AJP chairs the UK Department of Health and Social Care's (DHSC) Joint Committee on Vaccination and Immunisation (JCVI) and is a member of the World Health Organization's (WHO) Strategic Advisory Group of Experts. The views expressed in this manuscript are those of the author and do not necessarily reflect the views of the JCVI, DHSC, or WHO

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EDITOR'S NOTES

The Editor wishes to thank Professor Gerry Gormley for his immense contribution to the Journal over the last few years as Sub-Editor of the Curiositas section and for encouraging trainees to become involved in the production of the Journal. Curiositas will continue under the guidance of Drs. Paul Hamilton and Ian Bickle.

The Editor is mindful that his "tour of duty" ends after publication of the December 2019 edition of the Journal and therefore seeks a Deputy Editor to assist with producing the Journal with a view to taking over as Editor from 2020. Please contact the editor via e-mail at john.purvis@btinternet.com if you are interested.

ULSTER MEDICAL SOCIETY LECTURE PROGRAMME 2018-19

Presidential Address by Dr RG Peter Watson BSc MD FRCP FAoME: "What is a Physician?" on Thursday 4 October 2018 at 8 pm - venue to be confirmed

Full details of the UMS Lecture Programme 2018-19 to follow