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Placing the burden of bacteraemia in perspective

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Recognition of bacteria in the blood was one of the earliest advances of the 'bacteriological revolution' in the 19th century. The very existence and nature of bacteria was still challenged at that time, and the work by the French physician C. F. Davaine (1812–1882) stood out among other contributions. In a series of elegant experiments, Davaine proved that anthrax was caused by bacteria: first through direct visualization of the bacteria in the blood of sick animals by microscopy; then by infecting animals by injection of highly diluted blood from sick animals; and finally by infecting animals with bacteria sedimented from diluted blood by gravity, while inoculation of clear liquid from the surface was harmless [1,2]. The term bacteraemia (*bactériémie*) was coined in 1872 by another French physician, Edmé Vulpian (1826–1887), to emphasize the dissemination of the pathogen in the blood [1]. Bacteria and fungi had not yet been assigned to separate kingdoms, and thus, generically, bacteraemia also covers fungaemia. Bloodstream infection was already an established term in the 1920s, and was preferentially used in parturient and surgical patients, and later in infection control. From the beginning of the 20th century, blood cultures had become a practical diagnostic tool at major hospitals in North America and Europe. Bacteraemia research has since diversified to cover an ever-growing list of aetiological agents, as well as different patient groups, clinical settings, modes of acquisition, and, not least, the challenges of antibiotic resistance.

The articles by Laupland [3] and Goto and Al-Hasan [4] in this issue of the journal are important in a societal perspective, because they provide compelling data on the overall incidence and mortality of bacteraemia. Laupland reports on the population-based incidence of bacteraemia, showing an incidence range of 80 to approximately 190 episodes per 100 000 population per year, and a probable increase over time in the absolute incidence values and in the percentage of nosocomial cases. Goto and Al-Hasan [4] proceed further to evaluate the population mortality associated with bacteraemia. Extrapolating from existing reports, they estimate at least 75 000 deaths yearly in North America and 157 750 in Europe following bacteraemia, based on the lowest estimates of bacteraemia incidence and mortality. These estimates place bacteraemia alone in the top eight causes of death in many European countries and North America. However, these figures are derived from studies reporting on short-term mortality following bacteraemia, and the burden of bacteraemia is probably broader. Leibovici reviews the long-term consequences of bacteraemia among survivors, which are not negligible [5]. These translate to increased long-term mortality as compared with the general population, and cognitive and functional decline following the bacteraemia episode.

The major limitations of the data that we have on the burden of bacteraemia relate to the ability of existing systems to capture all cases in a defined population and the definitions of an episode of bactraemia [6]. Even with the most exhaustive inclusion methods, some patients may be missed, simply because the detection of microorganisms in blood depends on a timely decision to obtain blood for culture. As Laupland mentions, defining the population incidence mandates identification of all cases, but also exclusion of cases that do not belong to the population examined [3]. Indeed, selection and information bias can be seen as the 'Scylla and Charybdis' of bacteraemia research. The definitions and methods of assigning clinical significance to growth of bacteria in blood (as opposed to contamination) are variable in existing studies. In this issue, Kirn and Weinstein [7] provide an update on the definition of bacteraemia and the methods used to obtain, process and interpret blood cultures, which might help to standardize practice and research. Finally, the attribution of polymicrobial bacteraemia [8] and the assignment of continuous or relapsing bacteraemia are not uniform. The temporal limits of individual bacteraemic episodes have varied considerably among studies, and this had a significant impact on numbers of recurrences and thus total numbers of bacteraemias [9].

Where do we go from Here?

Despite the difficulties, epidemiological surveillance and population-based studies should continue to be an important

means of evaluating trends in bacterial epidemiology and the burden of infection. Standardization of definitions and methods can improve the quality of the data and comparability between studies. Surveillance systems, such as that for central-line-associated bloodstream infections [10], should be devised for all bloodstream infections. However, as observed by Goto and Al-Hasan, surveillance systems might exaggerate incidence values, owing to referral bias. Thus, efforts must be made to include all types of hospitals in such surveillance systems. The most appropriate sources of information on bloodstream infections are the electronic information systems used by clinical microbiology laboratories. Although additional clinical data are highly desirable, surveillance and research data can be obtained by the use of robust algorithms [11–13]. Already in 1969, Martin envisaged a national bacteraemia registry in the USA [14]. A few countries, such as Finland, Denmark, and the UK, have national registries [15–17]; however, these are still rare.

As well as constituting a window on the burden of sepsis, research based on bacteraemia has provided and will continue to provide an important means of examining the management of sepsis. A simple merit of bacteraemia is the possibility of evaluating the outcome of antibiotic therapy, as the causative agents and their susceptibility patterns are always known. Another important merit is the simplicity of including patients from a wide variety of clinical specialties and in diverse settings. Studies on new antibiotics or other interventions should focus on bacteraemia rather than on skin/soft tissue or abdominal infections.

Better Management of Bloodstream infections

Mortality rates following bacteraemia have not decreased in recent years; rather, the increase in the proportion of nosocomial cases might have resulted in an increase in the population mortality related to bacteraemia [3,4]. To decrease the global burden of bacteraemia, prevention and improved management are necessary. Early appropriate antibiotic treatment has repeatedly been shown to decrease mortality, but is only achieved in approximately 70% of patients with bacteraemia, with no significant improvement with time [18,19]. There is a delicate balance between the knowledge that early appropriate antibiotic treatment improves survival, but that unnecessary antibiotic treatment will trigger antibiotic resistance, and thus broad-spectrum antibiotic treatment for all is non-sustainable. With increasing numbers of multidrug-resistant bacteria, the latter part of this balance is receiving increasing attention and weight. Improved sensitivity of the microbiological methods would allow exclusion of bacterial infection and discontinuation of antibiotics when they are not needed. Methods for rapid detection and bacterial identification, such as matrix-assisted laser desorption ionization time-of-flight mass spectrometry, would allow for earlier directed antibiotic treatment [20]. The incorporation of decision support could improve the rates of appropriate empirical antibiotic treatment and result in a better, explicit balance between the ecological costs and the benefits of antibiotic treatment, leading to more judicious antibiotic prescription [21,22]. Hopefully, a combination of these technologies will succeed in curbing the increasing burden of sepsis and bacteraemia.

Transparency Declaration

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