Introduction to Pathogenic Bacteria

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Abstract

This chapter is a brief introduction to pathogenic microorganisms and also discusses virulence factors. An understanding of virulence factors is important, as they represent potential targets for the detection of microbial pathogens. Sources and routes of infection are also briefly discussed with reference to specific examples. There are a number of ways in which infection could be acquired, including via contaminated food and water; hospital acquired infection; “naturally acquired” infection; and intentional infection, for example, through the use of biological warfare agents. The focus of the review is predominantly on human pathogens. However, there are a range of other microbial pathogens of particular importance in other areas; for example, animal and plant pathogens, which will not be discussed. Finally, a brief overview of the detection of pathogenic bacteria is presented.

1. Pathogenic Microorganisms

Over many years there has been considerable debate as to the exact definitions of pathogenicity and virulence. These two words are often used interchangeably, but pathogenicity has been defined as the ability of an organism to cause disease and virulence as the relative severity of the disease caused by the organism (Watson and Brandly 1949). It has become increasingly apparent that virulence is highly complex and is dependent on the interaction between the host and the microorganism (Casadevall and Pirofski 2001). Taking into account the problems associated with defining virulence, virulence factors have also been difficult to characterise. Two definitions that have been put forward are that a virulence factor is (1) a “component of a pathogen that when deleted specifically impairs virulence but not viability” (Wood and Davis 1980); or (2) a “microbial product that permits a pathogen to cause disease” (Smith 1977). However, these often do not apply to infections caused by commensal or opportunistic pathogens, where often classic virulence determinants do not exist. Furthermore, the definitions may not account for host tissue damage that has been caused by the induction of a particular part of the host’s immune response, such as cytokine synthesis (Henderson et al. 1996). Therefore an understanding of virulence factors is important, as these can often be used to specifically detect pathogenic microorganisms. Classical virulence factors include factors that aid in a number of stages of infection:

1) host cell attachment;
2) entry to the host cell;

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3) evasion of detection by the hosts immune system;
4) intracellular or extracellular replication and inhibition of phagocytosis.

Virulence factors can be either requisite, where the gene products discriminate between pathogenic and nonpathogenic species; or contributory factors, that alter the severity of the disease. Again, the ability to cause disease and its severity will also be dependent on the immune status of the host. Contributory virulence factors do not fulfil the definition of virulence factors; nor do they separate pathogenic from nonpathogenic species, as they may be found in a wide range of microorganisms but still have a role in damage to host cells. A general consensus of opinion has been that regardless of the function of a gene product, if its expression leads to damage of the host cell then it is a virulence factor. Therefore Casadevall and Pirofski (1999) suggest that virulence factors should be defined as “attributes that mediate host damage.” Bacterial pathogens usually possess a number of virulence factors that are essential in establishing infection and causing disease. Classical virulence factors include toxins, as well as molecules that are involved in adherence, invasion of the host, evasion of the host’s immune response, and iron acquisition.

1.1. Toxins

Some microorganisms (e.g., *Bacillus anthracis*) produce toxins that are the major cause of clinical symptoms observed in patients. Toxins can be integral parts of the bacterium, such as lipopolysaccharide (endotoxins), or secreted molecules (exotoxins). Toxins often perform other functions, such as the making of adhesins (Tuomanen and Weiss 1985). Toxin secretion may also be regulated as part of an orchestrated response by the bacterium. The lipopolysaccharide (LPS) content of pathogenic Gram-negative cell walls is contained within a microorganism and usually released when the cell dies or is broken down (by autolysis or by the host’s immune response).

Unlike exotoxins, endotoxins are believed not to have any direct enzymatic action; and it is the lipid A portion, usually embedded within the bacterial membrane, that is believed to be the toxic component. As LPS is released from the bacterial cell, a number of host molecules involved in the inflammatory response are released (e.g., cytokines). One of the most important cytokines released is tumour necrosis factor-α (TNF-α). This molecule usually prevents the spread of a localised infection. However, the rapid stimulation of high levels of TNF-α within the bloodstream results in fever, damage to host tissue, an alteration of metabolism, and the production of further cytokines (IL-6, IL-8, IL-1, and PAF, platelet activating factor). These cytokines produce further damage to host cells and tissue resulting in a dramatic decrease in blood pressure and reduced blood flow to major organs leading to multiple organ failure (Tracey and Cerami 1993, Rink and Kirchner 1996). Exotoxins can be divided into a number of broad categories summarised below.

1.2. Adherence

Another important factor in establishing an infection is the ability of a microorganism to attach to a host cell or to an extracellular matrix. The macromolecules and structures involved in specific attachments to host cell receptors are often referred to as adhesins. Proteinaceous adhesins can be classified into two groups: afimbrial adhesins (sometimes termed nonpilus adhesins) and fimbriae (or pili). However, not all adhesins are essential for microbial virulence (Krogfelt 1991).

Fimbrial adhesins or pili can be observed by electron microscopy as hair-like structures that are present predominantly on the surface of Gram-negative bacteria (nearly all Gram-positive organisms do not possess pili). A number of Gram-negative pathogens utilise pili for adherence such as *Vibrio cholerae* and *Neisseria gonorrhoeae*. Originally it was suggested