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Virulence and Pathogenicity of Major Bacterial Pathogens Tome 1: Gram-Positive Pathogens

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1 Virulence and Pathogenicity of Major Bacterial Pathogens

1.1. Definitions and Conceptual Frameworks of Virulence and Pathogenicity

Virulence is commonly defined as the degree to which a microorganism causes damage in a susceptible host, whereas pathogenicity refers to the capacity of an organism to cause disease at all, implying that pathogenicity is a qualitative property and virulence is a quantitative one that varies with host context, inoculum, and route of entry (Casadevall & Pirofski, 2003; Finlay & Falkow, 1997).

Figure 1.1 provides an integrative schematic of the main causal frameworks used to define and measure virulence and pathogenicity across pathogens and host contexts (Casadevall & Pirofski, 2003; Falkow, 1988).

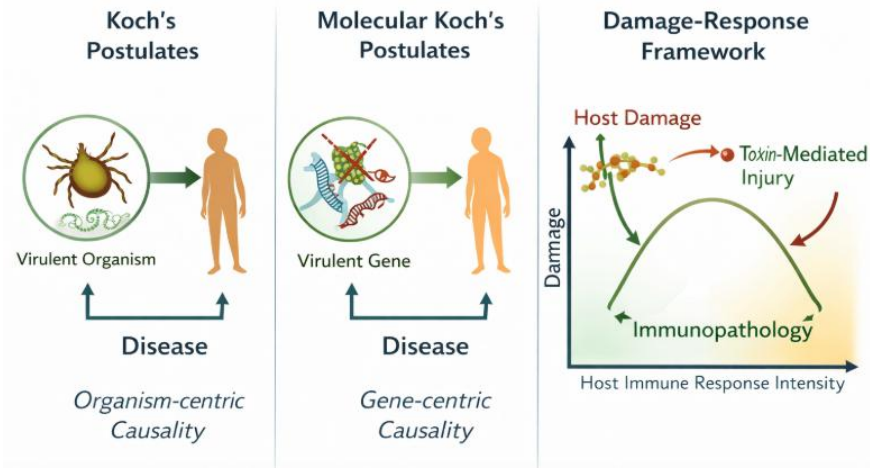

Figure 1.1. Conceptual frameworks for virulence and pathogenicity.

A pathogen can therefore be understood as an organism whose colonization or invasion of host tissues is associated with measurable impairment of host function or survival, while a commensal is an organism that persists with little to no net host damage under ordinary conditions; importantly, the same species may occupy either category depending on host immune status, anatomical site, and microbiota composition, a distinction that underlies opportunistic infections (Casadevall & Pirofski, 2003; Janeway & Medzhitov, 2002).

To avoid conflating bacterial presence with disease, it is useful to separate colonization (establishment and persistence on a body surface), infection (microbial replication in or on the host with engagement of host defenses), and disease (clinical signs and symptoms resulting from host damage). Quantifying virulence in experimental settings typically requires explicit endpoints, such as host survival curves, clinical scoring, histopathology, or measures of pathogen burden, and should distinguish direct toxin-mediated injury from inflammation-driven pathology (Casadevall & Pirofski, 2003; Medzhitov, 2007).

Historically, Koch's postulates provided a causal framework for linking microbes to disease, but their strict form is limited for polymicrobial infections, uncultivable organisms, and diseases in which host immune responses are major drivers of pathology. Molecular Koch's postulates, proposed to connect specific genes to pathogenic phenotypes, extended causality from the organism to defined genetic determinants by requiring that disruption of a candidate gene attenuates virulence and that genetic complementation restores it, with appropriate controls for polar effects and growth defects (Falkow, 1988).

The damage-response framework formalizes the idea that host damage can arise from both microbial factors and host immune responses, predicting that both insufficient and excessive immune activity can

increase damage and that virulence cannot be interpreted without specifying host immune status. This framework is particularly useful for comparing extracellular toxin-mediated diseases with intracellular infections in which immunopathology, such as granulomatous inflammation or cytokine-mediated tissue injury, is a dominant determinant of clinical outcome (Casadevall & Pirofski, 2003; Medzhitov, 2007).

Operational measurements, such as the infectious dose 50% (ID_{50}) or lethal dose 50% (LD_{50}), illustrate the dependence of virulence on route and host background, but they should be interpreted as model-specific parameters rather than intrinsic constants. Robust inference requires experimental designs that control inoculum viability, growth phase, and genetic background, and that incorporate blinded outcome assessment and sufficient biological replication to account for inter-individual host variability (Finlay & Falkow, 1997; Pizarro-Cerda & Cossart, 2006).

1.2. Classes of Virulence Factors: Adhesins, Invasins, Toxins, and Immune Modulators

Virulence factors are microbial molecules or structures that contribute to colonization, invasion, immune evasion, or host damage, typically without being required for basic viability in all environments. Their functions often depend on the anatomical niche, with Gram-negative pathogens frequently relying on specialized secretion systems to deliver effectors, and Gram-positive pathogens often deploying surface-anchored proteins and secreted toxins that act extracellularly (Finlay & Falkow, 1997; Costa et al., 2015).

Adhesins mediate attachment to host cells or extracellular matrix and thereby define tissue tropism and the initial spatial organization of infection. In Gram-negative bacteria, adhesins often include fimbrial or