

# Shigella flexneri

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## Shigella flexneri

Shigella flexneri, a facultative anaerobe belonging to the family Enterobacteriaceae, is a Gram-negative rod that is the causative agent of diarrhea and dysentery in humans. Potentially life-threatening, S. flexneri's effects include bacteremia, hemolytic uremic syndrome (HUS) and toxic megacolon (4). The principle disease of diarrhea and dysentery caused by this pathogen is known as shigellosis. 10-100 organisms are sufficient to cause disease, and transmission is generally from person-to-person by way of fecal-oral (2). Shigellosis can be characterized as a disease with over 60% [incidence](#) in children ages 1-5 (6).

### Life cycle:

S. flexneri causes infection via bacterial [penetration](#) of the mucous membrane in the human colon. Humans are the only known reservoir to this pathogen (7). Following invasion of M cells and upon contact with the epithelial cells of the colon, S. flexneri releases Ipa proteins through a type three secretion system. Once inside the host cell, Ipa proteins activate small GTPases in the Rho family as well as c-src, a protooncogene,

leading to cytoskeletal rearrangements. This [alteration](#) to the cytoskeleton allows the bacteria to be macropinocytosed by the host cell. Once inside the host, the pathogen colonizes the cytoplasm. IcsA, a bacterial surface protein, activates the host protein N-WASP and, in turn, stimulates actin assembly by host Arp 2/3. Thus, *S. flexneri* develops actin-based motility enabling the pathogen to become efficient at cell-to-cell spread and host cell cytoplasmic colonization. Infected cells become highly proinflammatory and secrete IL-8. IL-8 attracts neutrophils to the site of infection. The influx of neutrophils, chemokines and cytokines to the area damages the epithelial layer permeability and, in turn, advocates further *S. flexneri* invasion (6). Once initial invasion of *S. flexneri* occurs, the targeted epithelial cells require 45 minutes to 4 hours to mount an inflammatory response (8).

A diagram outlining *S. flexneri*'s type three secretion system can be viewed at:  
<http://www.grad.ucl.ac.uk/comp/2003/jointposter/gallery/index.pht?entryID=29>

Virulence:

A 214-kb virulence plasmid encodes for *S. flexneri*'s entry into human epithelial cells and intra-intercellular movement (6). Once in contact with the target cell, Ipa proteins (IpaB, IpaC and Ipa D) encode for a specific type III secretion system, thus, enabling entry of the pathogen into the target cell and characterizing *S. flexneri* with an invasive phenotype (1). One 30-kb block of the plasmid contains genes at the ipa/mxi-spa locus.

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