5.3: The Ability to Invade Host Cells

Skills to Develop

1. Briefly describe the mechanism by which invasins enable certain bacteria to enter host cells and state how this can promote colonization.
2. Briefly describe how a type 3 secretion system might be used to invade and survive inside host cells.
3. State how certain pathogenic spirochetes such as *Treponema pallidum* and *Borrelia burgdorferi* use adhesins, invasins and motility to penetrate host cells.

Highlighted Bacterium

1. Read the description of *Shigella* and match the bacterium with the description of the organism and the infection it causes.
2. Read the description of *Salmonella* and match the bacterium with the description of the organism and the infection it causes.
3. Read the description of *Borrelia burgdorferi* and match the bacterium with the description of the organism and the infection it causes.

Some bacteria produce molecules called invasins that activate the host cell's cytoskeletal machinery enabling bacterial entry into the cell by phagocytosis. Advantages of entering a human cell include (1) providing the bacterium with a ready supply of nutrients and (2) protecting the bacteria from complement, antibodies, and other body defense molecules.

Flash animation of bacteria secreting invasins in order to penetrate non-immune host cells.

html5 version of animation for iPad of bacteria secreting invasins in order to penetrate
In addition, some pathogenic bacteria invade phagocytic cells, neutralize their killing ability, and turn them into a safe haven for bacterial replication (Figure 5.3.1). Some bacteria also kill phagocytic dendritic cells once they are engulfed and prevent those dendritic cells from activating the T4-lymphocytes and T8-lymphocytes required for adaptive immunity.

**Figure 5.3.1: Salmonella Surviving Inside Macrophages.** Once in the phagosome of the macrophage the bacterium uses its type 3 secretion system to inject proteins that prevent the lysosomes from fusing with the phagosomes, thus providing a safe haven for Salmonella replication within the phagosome and protecting the bacteria from antibodies and other defense elements.

Invasins of *Salmonella*, *Shigella*, and enteroinvasive strains of *Escherichia coli* (EIEC), for example, allow these bacteria to enter epithelial cells of the colon. These bacteria, like many involved in infection, have the ability to co-opt the functions of the host cell for the bacterium’s own benefit. This is done by way of bacterial secretions systems that enable the bacterium to directly inject bacterial effector molecules into the cytoplasm of the host cell in order to alter its cellular machinery or cellular communication.

The most common type is the type 3 secretion system (Figure 2). A secretion apparatus in the cytoplasmic membrane and cell wall of the bacterium polymerizes a hollow needle that is lowered to the cytoplasmic membrane of the host cell and a translocon protein is then delivered to anchor the needle to the host cell. Effector proteins in the bacterium can now be injected into the cytoplasm of the host cell. The delivery system is sometimes called an *injectosome*. 
Figure 2: The Bacterial Type 3 Secretion System. Many bacteria involved in infection have the ability to co-opt the functions of the host cell to the benefit of the bacterium. This is done by way of bacterial secretions systems that enable the bacterium to directly inject bacterial effector molecules into the cytoplasm of the host cell in order to alter its cellular machinery or cellular communication. The most common type is the type 3 secretion system. A secretion apparatus in the cytoplasmic membrane and cell wall of the bacterium polymerizes a hollow needle that is lowered to the cytoplasmic membrane of the host cell and a translocon protein is then delivered to anchor the needle to the host cell. Effector proteins in the bacterium can now be injected into the cytoplasm of the host cell. The delivery system is sometimes called an injectisome.

When these bacteria contact the epithelial cells of the colon, the type III secretion system delivers proteins into the epithelial cells enabling them to polymerize and depolymerize actin filaments. This cytoskeletal rearrangement is a key part of the pseudopod formation in phagocytic cells and is what enables phagocytes to engulf bacteria and place them in a vacuole. Thus the bacterium with its invasins is able to trick the epithelial cell into behaving like a phagocyte and engulfing the bacterium. The bacteria then replicate within the host cell.

We will now look at several examples of bacteria that use invasions to invade host cells.

1. It is thought that *Shigella* first transit the mucous membrane of the colon by passing through M cells. (M cells are phagocytic cells in the mucous membrane whose function is to sample microbes from the intestinal lumen and pass them on to the lymphoid tissue of the Peyer's patch in order to activate the immune defenses against intestinal microbes). Once across the mucosa, the *Shigella* use a type 3 secretion system to inject invasins into the underside of the epithelial cells to induce phagocytic uptake of the bacterium (see Figure 3).
Once inside they escape from the vacuole into the cytoplasm and multiply. Once inside, *Shigella* produces a protease that cleaves tubulin, a major component of the microtubule cytoskeleton. The microtubules represent a barrier to bacterial movement within the infected cell and the protease breaks down this barrier.

Now they move through the host cell and spread to adjacent host cells by a unique process called actin-based motility whereby actin filaments polymerize at one end of the bacterium producing comet-like tails that propel the *Shigella* through the cytoplasm of the host cell. When they reach the boundary of that cell, the actin filaments push the *Shigella* across that membrane and into the adjacent cell (Figure 5.3.3). Actin-based motility enables the bacteria to spread from cell-to-cell without having to encounter defense cells and antibodies. As the *Shigella* grow and spread within the epithelial cells, those epithelial cells die and provoke a strong inflammatory response leading to the symptoms of dysentery.

![Figure 5.3.3: Shigella Passing Through the Mucous Membrane and Invading Mucosal Epithelial Cells Via M-Cells. A proposed model for invasion of epithelial cells of the colon. 1) The Shigella first cross the mucosa by passing through specialized cells called M cells. The M cell passes the Shigella on to a dendritic cell. 2) The Shigella subsequently escapes from the dendritic cell by inducing apoptosis, a programmed cell suicide. 3) The Shigella then uses its invasins to enter the mucosal epithelial cells from underneath. The invasins cause actin polymer rearrangements in the cytoskeleton of the host cell resulting in the bacterium being engulfed and placed in an endocytic vesicle in a manner similar to phagocytic cells. Once inside, the Shigella escape from the vacuole into the cytoplasm and multiply. 4) The Shigella are able to move through the host cell and spread to adjacent host cells by a unique process called actin-based motility. In this process, actin filaments polymerize at one end of the bacterium, producing comet-like tails that propel the Shigella through the cytoplasm of the host cell. 5) When they reach the boundary of that cell, the actin filaments push the Shigella across that membrane and into the adjacent cell.](https://bio.libretexts.org/Bookshelves/Microbiology/Book%3A_Microbiology_(Kaiser)/Unit_3%3A_Bacterial_Pathogenesis/5%3A...
intestinal wall to the underside. It then uses its type 3 secretion system to inject effector proteins from the phagosome into the cytoplasm. These proteins trigger apoptosis or cell suicide of the dendritic cell. Killing the dendritic cells prevents them from presenting *Shigella* to T4-lymphocytes, a step required for the production of antibodies against the *Shigella* (see Figure 4).

- For a movie showing *Shigella* being propelled by actin-based motility within a cell, see the Theriot Lab Website at Stanford University Medical School. Click on "Greatest Hits" and then on "*Shigella flexneri* associated with actin tails in PtK2 cells."

2. *Salmonella* use a type 3 secretion system to inject intestinal epithelial cells with effector proteins that stimulate actin re-arrangement and cause the epithelial cell's cytoplasmic to "ruffle" up and engulf the bacteria Figs. 5A - Figure 5B. The *Salmonella* pass through the epithelial cell where they are engulfed by phagocytic macrophages.

Once in the phagosome of the macrophage the bacterium uses its type 3 secretion system to inject proteins that prevent the lysosomes from fusing with the phagosomes, thus providing a safe haven for *Salmonella* replication within the phagosome and protecting the bacteria from antibodies and other defense elements (see Figs. 5C-5D).

By injecting flagellin into the cytoplasm of the macrophage the *Salmonella* can also eventually kill the macrophage by inducing apoptosis, a programmed cell suicide.

Molecules injected into the intestinal epithelial cells also stimulate diarrhea. Advantages of inducing diarrhea include (1) flushing out normal flora bacteria so there is less competition for nutrients; and (2) better enabling *Salmonella* that are not attached to host cells to be transmitted to a new host via the fecal-oral route.

For a movie showing *Salmonella* invading a human cell, see the Theriot Lab Website at Stanford University Medical School. Click on "Greatest Hits" and then on "*Salmonella typhimurium* invading a fibroblast cell."

Highlighted Bacterium: *Salmonella*

https://bio.libretexts.org/Bookshelves/Microbiology/Book%3A_Microbiology_(Kaiser)/Unit_3%3A_Bacterial_Pathogenesis/5%3…
Click on this link, read the description of *Salmonella*, and be able to match the bacterium with its description on an exam.

3. *Listeria monocytogenes* is another bacterium that enters intestinal cells via invasins and spreads to adjacent cells by actin-based motility. Its actin-based motility enables it to move approximately 1.5 µm per second within the host cell.

For movies showing *Listeria* entering host cells and being propelled by actin-based motility within a cell, see the Theriot Lab Website at Stanford University Medical School. Click on "Greatest Hits" and then on "Life history of a single infecting *Listeria monocytogenes*" and "*Listeria monocytogenes* moving in PtK2 cells."

4. Although enteroinvasive *Escherichia coli* (EIEC) don't have actin-based motility, they invade and kill epithelial cells of the colon in a manner similar to *Shigella*.

5. *Legionella pneumophila*, after being ingested by macrophages and placed in a phagosome, uses a type 4 secretion system to inject effector proteins that prevent the lysosomes from fusing with the phagosomes and turning the macrophage into a safe haven for bacterial replication. The same mechanism allows the *Legionella* to survive inside amoebas in nature. These amoebas serve as a reservoir for the bacterium in the environment.

6. F protein and M-protein of *Streptococcus pyogenes* (Group A beta streptococci) enables the bacterium to invade epithelial cells. This is thought to help maintain persistent streptococcal infections and enable the bacterium to spread to deeper tissues.

7. The spirochete *Borrelia burgdorferi* probably uses a combination of invasins and motility to penetrate host cells. In this case the host cell doesn't phagocytose the bacterium. Instead, one tip of the spirochete attaches to the host cell and some form of invasin apparently causes the host cell to release digestive enzymes that enable the spirochete with its corkscrewing motility to penetrate the host cell membrane. Once in the host cell the bacteria may remain dormant for years and hide from the immune system and antibiotics.

8. Another spirochete, *Treponema pallidum*, is thought to enter cells in a similar fashion. Motility also helps *B. burgdorferi* and *T. pallidum* to invade and leave blood vessels by passing between and through endothelial cells, thus enabling the spirochetes to disseminate to other locations in the body.

Click on this link, read the description of *Borrelia burgdorferi*, and be able to match the bacterium with its description on an exam.

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**Electron micrograph of Treponema pallidum invading a host cell.**

**Highlighted Bacterium: Borrelia burgdorferi**

Click on this link, read the description of *Borrelia burgdorferi*, and be able to match the bacterium with its description on an exam.

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**Flash animation showing spirochetes using motility and invasins to enter a blood vessel.**

**html5 version of animation for iPad showing spirochetes using motility and invasins to**
Exercise: Think-Pair-Share Questions

Bacteria such as *Salmonella*, and *Shigella* routinely enter intestinal epithelial cells.

Briefly describe how they enter the epithelial cell and state 2 advantages this might provide the bacterium in terms of its pathogenicity.

E-Medicine article on infections associated with organisms mentioned in this Learning Object. Registration to access this website is free.

- *Shigella species*
- *Listeria monocytogenes*
- *Escherichia coli*
- *Salmonella species*
- *Pseudomonas aeruginosa*
- *Legionella pneumophila*
- *Yersinia enterocolitica*
- *Neisseria gonorrhoeae*
- *Borrelia burgdorferi*
- *Treponema pallidum*
- *Streptococcus pneumoniae*

**Summary**

Some bacteria produce molecules called invasins that activate the host cell's cytoskeletal machinery enabling bacterial entry into the cell by phagocytosis. Entering a non-defense host cell can provide the bacterium with a ready supply of nutrients, as well as protect the bacterium from complement, antibodies, and other body defense molecules. Some bacteria invade phagocytic cells, neutralize their killing ability, and turn them into a safe haven for bacterial replication. Some bacteria kill phagocytic dendritic cells once they are engulfed and prevent those dendritic cells from activating the T-lymphocytes required for adaptive immunity. These bacteria have the ability to co-opt the functions of the host cell for the bacterium's own benefit. This is done by way of bacterial secretions systems that enable the bacterium to directly inject bacterial effector molecules into the cytoplasm of the host cell in order to alter its cellular machinery or cellular communication.

**Contributors**

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