

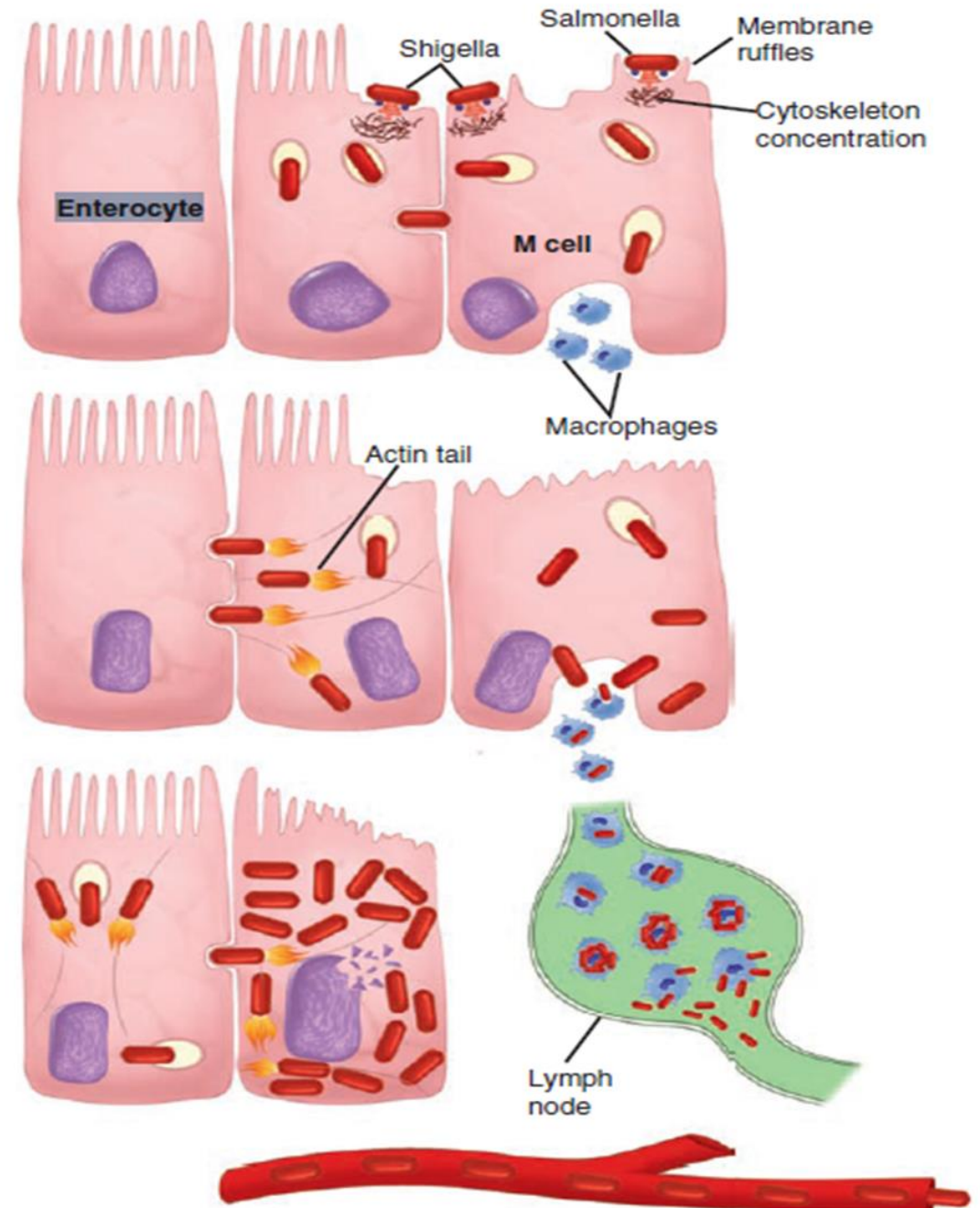


Salmonella

- Salmonellae
 - Typhi
 - Non-Typhi: *S enterica*
- Most strains are motile through the action of their flagella.
- **Salmonella Typhi has a surface polysaccharide called the Vi antigen,**

- Salmonella gastroenteritis is predominantly a disease of **industrialized societies**
 - improper food handling, which allows the transmission from the animal reservoir to humans.
 - The infecting dose of *S enterica* infection varies widely with the serotype (200-10⁶ bacteria), but is generally considerably **higher than Shigella**.

- Ingestedpass the stomach acid
...the intestinal mucous layer ... reach the small bowel.
- the initial contact there is with M cells, enterocytes, or both.....mediated by pili.
- injection (type III) secretion systems, the creation of membrane “ruffles” dramatically alters the normal host cell architecture within minutes



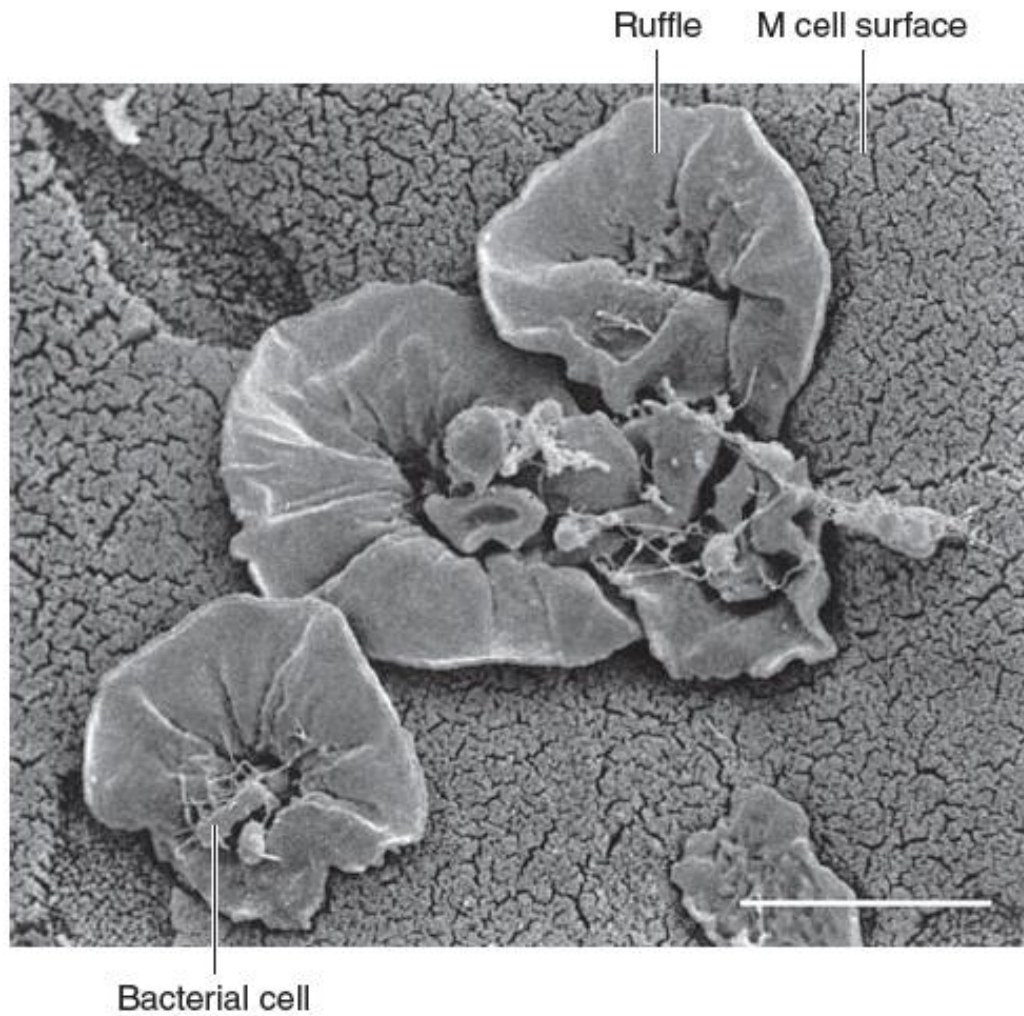
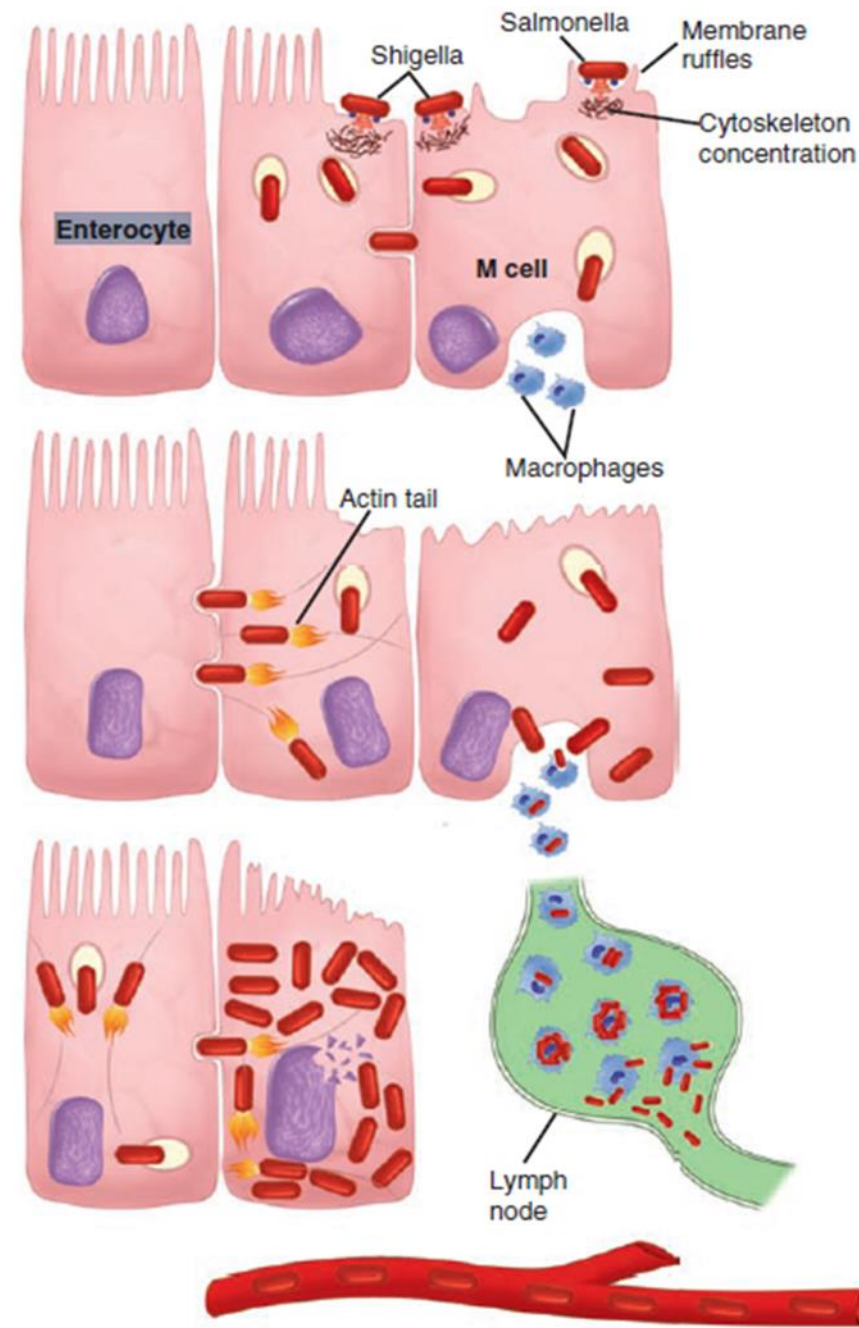


FIGURE 33-9. Salmonella ruffles. *S* serotype Typhimurium is shown inducing wave-like ruffles on an intestinal M cell. This leads to induction of uptake of the bacteria by the M cell. (Reproduced with permission from Nester EW: *Microbiology: A Human Perspective*, 6th edition, 2009.)

plasma membrane sites of filamentous actin cytoskeletal rearrangement normally induced by physiologic molecules such as growth factors.

- The ruffles..... engulf the organism in an endocytotic vacuole
.....transcytose from the apical surface to the basolateral membrane.
- Once in the cell, *S enterica* multiplies in a vacuole and continues on through the cell and entering the lamina propria.



- induce a profound inflammatory response
- phagocytosed by neutrophils and macrophages.
- Persistence in the lamina propria
- **remains localized to the mucosa and submucosa with most S enterica strains,**

Enteric (Typhoid) Fever (Salmoella Typhi)

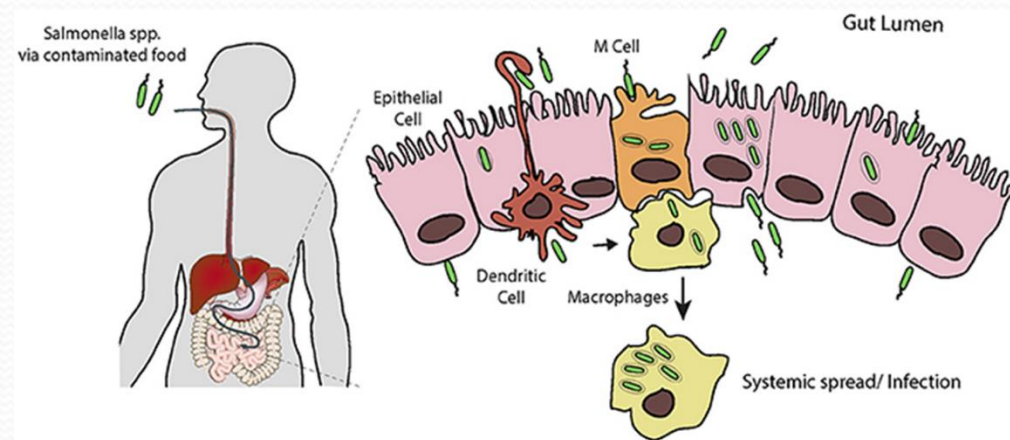
- Typhoid fever is a strictly human disease.
- **Chronic carriers** of serotype Typhi are the primary reservoir.
- Some patients become chronic carriers for years (hence the infamous “Typhoid Mary” Mallon), usually because of chronic infection of the biliary tract when gallstones are present..
- Mary Mallon, known commonly as Typhoid Mary, was an Irish-born American cook believed to have infected between 51 and 122 people with typhoid fever



- All cases can and should be traced back to their human source.
 - fecal–oral route.
- Three serotypes called **Paratyphi (A, B, C)** have features similar to **S Typhi**, including the production of an enteric fever syndrome.

Pathogenesis

- The invasion and killing of intestinal M cells and macrophages are presumed to follow the same pattern as that of *S. enterica*.
- **Two differences are the Vi surface polysaccharide and the extended multiplication of Typhi in macrophages.**



- Vi+ phenotype favors **intracellular multiplication**. Like other serotypes of Salmonella, Typhi remains within a membrane-bound vacuole, but unlike them, rather than killing the macrophage, it enters a stage of **extended replication**.
- The primary difference between Typhi and the other serotypes is the **prolonged intracellular survival in macrophages**.
 - ability to inhibit the oxidative metabolic burst and continue to multiply.
 - **lymphatic circulation**
 - mesenteric nodes, spleen, liver, and bone marrow, all elements of the reticuloendothelial system (RES).

- This sometimes results in metastatic infection of other organs including the **urinary tract and the biliary tree**.
- The latter causes reinfection of the bowel. This cycle beginning and ending in the small intestine takes approximately 2 weeks to complete.

Manifestation

- The clinical patterns of salmonellosis can be divided into
 - Gastroenteritis,
 - Bacteremia with and without focal extraintestinal infection,
 - Enteric fever (**multiorgan**)
 - The asymptomatic carrier state.

Enteric Fever

- Enteric fever is a **multiorgan**
- prolonged fever, sustained bacteremia, and profound involvement of the mesenteric lymph nodes, liver, and spleen.

- The mean incubation period is **13 days**,
- the first sign of disease is **fever** associated with a **headache**.
The fever rises in a stepwise fashion over the next 72 hours.
- A relatively **slow pulse** is characteristic and out of character with the elevated temperature.
- A faint rash (rose spots) appears during the first few days on the abdomen and chest.



- Many patients are **constipated**, although perhaps one-third of patients have a mild diarrhea.
- chronic infection of the bloodstream is serious, and the effects of endotoxin can lead to **myocarditis, encephalopathy, or intravascular coagulation**. Moreover, the persistent bacteremia can lead to infection at other sites.

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- Of particular importance is the **biliary tree**, with reinfection of the intestinal tract and diarrhea late in the disease.

- the most important complication of typhoid fever is **hemorrhage** from perforations through the wall of the terminal ileum or proximal colon at the site of necrotic Peyer patches. These occur in patients whose disease has been progressing for 2 weeks or more.



Diagnosis

- **Culture of Salmonella** from the blood or feces is the primary diagnostic method.
 - Early blood is far more likely to give a positive culture result than culture from any other site.
- **Failure to ferment lactose** and the production of **hydrogen sulfides** from sulfur-containing amino acids are characteristic features used to identify suspect colonies on the selective isolation media.

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- the use of antimicrobial agents in **S enterica** gastroenteritis is restricted to those with severe infections or underlying risk factors, particularly children.

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- Antimicrobial therapy is **clearly indicated in typhoid fever.**



Shigella

Shigella

- Closely related to E coli.
- lack flagella and thus H antigens.
- All Shigella species are nonmotile.
- The genus is divided into four species,

- *Shigella dysenteriae* (serogroup A),
- *Shigella flexneri* (serogroup B),
- *Shigella boydii* (serogroup C),
- *Shigella sonnei* (serogroup D).

- Shigella is the prototype **invasive** bacterial pathogen.
- Shigella dysenteriae type A₁, the Shiga bacillus, is the most potent producer of Stx.
- Other Shigella species produce various molecular forms and quantities of Stx.

Epidemiology

- Shigellosis is a strictly human disease with no animal reservoirs.
- Worldwide, it is consistently one of the most common causes of infectious diarrhea
- Shigella disease remains important in both developed and developing countries.

- The fecal–oral route.
 - person-to-person contact is **so effective**
 - the infecting dose is extremely low, as few as **10 organisms in some studies.**
- The secondary attack rates among family members are as high as 40%.
- Shigella is also spread by food or water contaminated by humans.

Pathogenesis

- **Acid-resistant** and survives passage through the stomach to reach the intestine **invasion** and destruction of the human **colonic mucosa**.
- This triggers an intense acute **inflammatory** response with mucosal **ulceration** and **abscess** formation.

- The diarrhea created by this process is almost purely **inflammatory**, consisting of small-volume stools containing **WBCs**, **RBCs**, bacteria, and little else. This is classic **dysentery**.
- The disease remains localized to the colonic mucosa. Spread to the bloodstream is uncommon.


- Some *Shigella* also produce **Stx**, which is not essential for disease, but does contribute to the severity of the illness.
 - The original and most potent producer of Stx, *S. dysenteriae* type 1,
 - significant mortality rate in previously healthy individuals.
 - systemic effects of the **toxin and HUS**.

Manifestation

- acute inflammatory colitis and bloody diarrhea, which in the most characteristic state presents as a **dysentery syndrome**—a clinical triad consisting of
 1. **cramps**
 2. painful straining to pass stools (**tenesmus**),
 3. a frequent, **small-volume, bloody, mucoid fecal discharge**.

Treatment

- Usually self-limiting, the beneficial effect of treatment is in shortening the duration of the illness and the period of excretion of organisms.

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- Ciprofloxacin, ceftriaxone, and azithromycin have been used depending on susceptibility testing.
 - Antispasmodic agents may aggravate the condition and are contraindicated in shigellosis and other invasive diarrheas.