

1. Patient history: An apple a day...

An Apple a Day

A five year old previously healthy boy presents with new onset of bloody diarrhea. The patient had 4-5 bloody bowel movements on the day of presentation. The parents did not note any fever or chills. The patient complained of slight abdominal pain.

His past medical history was unremarkable. He had had all of the standard childhood immunizations. Approximately 5 days prior to the onset of symptoms, the family had visited a local apple orchard and had sampled some fresh apple cider. The father notes that there were many livestock in the area of the orchard.

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2. Patient history: An apple a day (cont.)

On PE, the child was afebrile with normal BP and pulse. The rest of the exam was unremarkable except for the rectal exam which revealed grossly blood stool.

Laboratory tests at the time revealed a positive test for fecal leukocytes. His hematocrit was normal at 40%. His WBC was elevated at 20,000.

The patient was discharged without any therapy other than a recommendation for oral hydration.

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3. EHEC: Course of disease (1)

EHEC: Course of disease

Encounter:	Undercooked meat products from processing plants--animals infected. Vegetables: parsley, lettuce (human or animal feces contaminated). Cider.
Entry:	Colonization of large intestine
Multiplication:	Directly attach to intestinal epithelium--unusual for <i>E. coli</i> strains

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4. EHEC: Course of disease (2)

EHEC: Course of disease

Spread:	Colonization of bacteria is localized, but damage is systemic
Damage:	1. Watery diarrhea 2. Bloody diarrhea 3. Haemolytic uraemic syndrome (HUS)

Damage appears mediated both by the colonization process (diarrheal disease) and by a toxin (systemic disease)

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5.

EHEC: Virulence Factors

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- 1. Intimin: Bacterial adhesin**
- 2. Tir: Receptor for intimin translocated to epithelial cell**
- 3. Shiga toxin (also known as verotoxin): responsible for HUS??????**

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6.

Bacterium

How does bacterium cause actin rearrangement?

- A. Bacterium has secretion machine that pumps proteins into host cell (called Type III secretion system).**
- B. A bacterial protein (called Tir) is deposited into the enterocyte plasma membrane.**
- C. A second bacterial protein called intimin binds Tir.**
- D. Tir focuses actin rearrangements.**

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7. EHEC: Course of disease (3)

EHEC: Course of disease

Spread: Colonization of bacteria is localized,
but damage is systemic

Damage:

1. Watery diarrhea
2. Bloody diarrhea
3. **Haemolytic uraemic syndrome (HUS)**

Is HUS Toxin-Mediated?

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8. E. Coli

Why is *E. coli* sometimes a pathogen?

1. Some strains have virulence factors that cause damage to intestine
 - a. Toxins (ETEC strains)
 - b. Factors promoting attaching and effacing lesions
 - c. Factors prompting bacterial entry into epithelium
2. Presence in some strains of virulence factors that allow extraintestinal colonization.
 - a. Urinary tract infections: specialized pili
 - b. Meningitis: encapsulated organisms (K1)

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9. Patient history...salad

Caesar's Revenge?

The patient is a 34 yo male with a history of AIDS who presents with a 12 hour history of nausea and vomiting followed by multiple episodes of diarrhea. The diarrhea is watery, but without any blood or mucous visible. Over the last 2 hours, he has noted the onset of fevers, chills and a slight headache. He presented to the emergency room when she began to develop increasing abdominal pain described as cramping.

The patient denies any sick contacts or recent travel. He has not eaten any unusual foods, but did have a Caesar's salad made with raw eggs ~48 hours prior to the onset of symptoms. He has a pet cat and a pet lizard.

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10. Patient history...salad (cont.)

His PE was notable for a fever of 102.5, pulse of 100 and RR of 15. His abdominal exam revealed tenderness to palpation in the lower quadrants with slight rebound and guarding. A rectal exam showed trace guaiac positive stools.

Laboratory data revealed a slightly elevated WBC of 12,000 and slightly decreased serum Na of 133. Fecal leukocytes were present on examination.

He was given IV hydration and started on ciprofloxacin.

Stool cultures sent from the ER grew *Salmonella choleraesuis*, subtype *typhimurium*. Blood cultures also positive for *Salmonella*.

The patient initially improved on ciprofloxacin, but when the antibiotic was discontinued after 2 weeks, he again became febrile with shaking chills.

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11. NTS: Course of disease

NTS: Course of disease

Encounter:	Undercooked meat products from processing plants--chickens, eggs.
Entry:	Colonization of small intestine (contrast with EHEC) and entry into cells within epithelial layer.
Multiplication:	Growth occurs in the subepithelial layers of small intestine. Probably occurs both extracellularly and within phagocytic cells

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12. NTS: Course of disease (cont.)

NTS: Course of disease

Spread:	In simple diarrhea, bacteria remain intestinally localized. This is unlike enteric fever induced by <i>S. typhi</i>
Damage:	Watery diarrhea

Damage appears mediated both by entry into the submucosal region and stimulation of inflammatory response resulting in Cl⁻ secretion by enterocytes.

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13.

NTS: Virulence Factors

NTS: Virulence Factors

1. **Products of *spi-1* (pathogenicity island 1): allow entry into epithelial cells, induction of cytokines and production of chemoattractants**
2. **Products of *spi-2* (pathogenicity island 2): allow survival in macrophages and disarming of O₂-dependent killing.**
3. **Flagella? May induce interleukin 8 secretion**

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14.

NTS: How is diarrhea caused?

NTS: How is diarrhea caused?

NOT KNOWN--but a Cl⁻ secretory response by epithelium is involved . . .

1. **Products of *spi-1* cause the induction of pro-inflammatory cytokines allowing directed migration of neutrophils through epithelium into lumen of intestine.**
2. **Products of *spi-2* allow proliferation of bacteria in submucosal and inflammatory response occurs that cannot clear infection**

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