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Non-Typhoidal Salmonellosis

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Overview

- Organism
- History
- Epidemiology
- Transmission
- Disease in Humans
- Disease in Animals
- Prevention and Control

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In today's presentation, we will cover information regarding the organism that causes non-typhoidal salmonellosis and its epidemiology. We will also talk about the history of the disease, how it is transmitted, species that it affects and clinical and necropsy signs observed. Finally, we will address prevention and control measures for non-typhoidal salmonellosis.

[Photo: Cow. USDA ARS, Peggy Greb]

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The Organism

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Salmonellosis

- Gram negative, facultative rod
- Two species
  - *S. bongori*
  - *S. enterica*
    - Six subspecies
- More than 2500 known serovars
  - Many zoonotic (non-typhoidal)

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Salmonella spp. are members of the family Enterobacteriaceae. They are Gram negative, facultatively anaerobic rods. The genus *Salmonella* contains two species, *S. enterica*, the type species, and *S. bongori*. *S. enterica*. contains six subspecies: *S. enterica* subsp. *enterica*, *S. enterica* subsp. *salamae*, *S. enterica* subsp. *arizonae*, *S. enterica* subsp. *diarizonae*, *S. enterica* subsp. *houtenae* and *S. enterica* subsp. *indica*. Within each subspecies are serovars; over 2500 serovars are presently known. Most of the isolates that cause disease in humans and other mammals belong to *S. enterica* subsp. *enterica*. A few serovars, *Salmonella* ser. Typhi, *Salmonella* ser. Paratyphi and *Salmonella* ser. Hirschfeldii are human pathogens that are transmitted from human to human. The remaining *Salmonella* serovars, sometimes referred to as non-typhoidal *Salmonella*, are zoonotic or potentially zoonotic.

[Photo: *Salmonella* spp. CDC Public Health Image Library]

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Importance

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History

- First isolated in 1884
  - *S. choleraesuis* in pig intestine
- Prevalence in the U.S.
  - 1980: 30,000
  - 1986: 42,028
  - 1998-2002: 128, 370
- Estimated 1.4 million cases/year
  - Only 40,000 culture-confirmed

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Salmonella was first discovered in 1884 by Dr. DE Salmon; he isolated the bacterium (*S. choleraesuis*) from the intestine of a pig. By 1980, more than 30,000 people were reported to be infected with *Salmonella* in the United States. This number increased to 42,028 by 1986. From 1998-2002, the CDC reported 128,370 cases. An estimated 1.4 million cases occur annually in the U.S., although only about 40,000 are culture-confirmed and reported to CDC.

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Epidemiology

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Geographic Distribution

- Worldwide
  - Related to animal husbandry
  - Wild reservoirs
- Serovar distribution varies
  - Some geographically limited
- Eradication programs in some countries
  - Sweden

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Salmonellosis can be found worldwide but seems to be most common where intensive animal husbandry is practiced. Reservoirs also remain in wild animals. Some *Salmonell*a are geographically limited. *Salmonella* eradication programs have nearly eradicated the disease in domestic animals and humans in some countries (e.g., Sweden).

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U.S. Serotypes, 2009

- Enteritidis
- Typhimurium
- Newport
- Javiana
- Heidelberg
- Montevideo
- 14,[5],12.i:-
- Muenchen

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The Foodborne Diseases Active Surveillance Network (FoodNet) is the principal foodborne disease component of CDC's Emerging Infections Program (EIP). The project consists of active surveillance for foodborne diseases and related epidemiologic studies designed to help public health officials better understand the epidemiology of foodborne diseases in the United States. States in yellow (figure, above) participate in FoodNet. In 2009, the most common *Salmonella* serotypes isolated from FoodNet were: Enteritidis, Typhimurium, Newport, Javiana, Heidelberg, Montevideo,14,[5],12.i:-, and Muenchen.

Image: States participating in FoodNet. CDC.

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Morbidity/Mortality: Animals

- Asymptomatic infections are common
  - 1-3% carriers
  - Higher in reptiles, birds
- Clinical disease
  - Young, pregnant/lactating, stress
  - Mortality can reach 100%

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In animals, asymptomatic *Salmonella* infections are common. Overall, approximately 1-3% of domestic animals are thought to carry *Salmonella* spp. but the prevalence can be much higher in some species. Among mammals, clinical disease is most common in very young, pregnant or lactating animals, and usually occurs after a stressful event. Outbreaks with a high morbidity rate and sometimes a high mortality rate are typical in young ruminants, pigs, and poultry. In outbreaks of septicemia, morbidity and mortality can reach 100%.

[Photo: Sow with litter. USDA ARS]

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Prevalence in Animals

	86%
	50%
	1-36%
	2-20%
	6%

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Estimates of the carrier rate among reptiles vary from 36% to more than 80-90%, and several serovars can be found in a single animal. Some authorities consider most or all reptiles to be *Salmonella* carriers. High prevalence rates can also be present in some birds and mammals. *Salmonella* spp. have been isolated from 41% of turkeys tested in California and 50% of chickens examined in Massachusetts. *Salmonella* spp. have also been isolated from 1-36% of healthy dogs and 1-18% of healthy cats in various studies, as well as 6% of beef cattle in feedlots. From 2-20% of horses are thought to be healthy shedders.

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Transmission

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Human Transmission

- Fecal-oral: direct or indirect
- Commonly contaminated items
  - Meat, eggs, water
- Fecal material from:
  - *Reptiles
  - *Chicks
  - *Ducklings
  - Livestock, dogs, cats, adult poultry

People are often infected when they eat contaminated foods of animal origin such as meat or eggs. They can also be infected by ingesting organisms in animal feces, either directly or in contaminated food or water. Directly transmitted human infections are most often acquired from the feces of reptiles, chicks and ducklings. Livestock, dogs, cats, adult poultry and cage birds can also be involved.

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Animal Transmission

- Fecal-oral
  - Carried asymptomatically
- Fomites, mechanical vectors
- Vertical
  - Birds
- *In utero*
- Contaminated food and water

Salmonella spp. are mainly transmitted by the fecal-oral route. They are carried asymptomatically in the intestines or gall bladder of many animals, and are continuously or intermittently shed in the feces. Vertical transmission occurs in birds, with contamination of the vitelline membrane, albumen and the yolk of eggs. *Salmonella* spp. can also be transmitted *in utero* in mammals. Animals may also become infected from contaminated feed (including pastures), drinking water, or close contact with infected animal (including humans). Birds and rodents can spread *Salmonella* to livestock. Carnivores are also infected through meat, eggs, and other animal products that are not thoroughly cooked.

[Photo: Chickens. USDA ARS, Stephen Ausmus]

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Non-Typhoidal Salmonellosis and Humans

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Disease in Humans

- Incubation period:
  - Gastroenteritis: 12 hrs to 3 days
  - Enteric fever: 10 to 14 days
- Asymptomatic to severe
- All serovars can produce all forms
  - Reptile-associated is most severe

In humans, salmonellosis varies from a self-limiting gastroenteritis to septicemia. Whether the organism remains in the intestine or disseminates depends on host factors as well as the virulence of the strain. Asymptomatic infections can also be seen. All serovars can produce all forms of salmonellosis, although a given serotype is often associated with a specific syndrome (e.g. *Salmonella choleraesuis* tends to cause septicemia). Salmonellosis acquired from reptiles is often severe, and may be fatal due to septicemia or meningitis. Most cases of reptile-associated salmonellosis are seen in children under 10 and people who are immunocompromised.

[Photo: Boy holding turtle. CDC, James Ganthany]

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Clinical Sign: Gastroenteritis

- Nausea, vomiting, cramping abdominal pain and diarrhea (may be bloody)
- Headache, fever, chills, myalgia
- Severe dehydration: infants, elderly
- Symptoms resolve in 1 to 7 days
- Sequela: Reiter's syndrome

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Gastroenteritis is characterized by nausea, vomiting, cramping abdominal pain and diarrhea, which may be bloody. Headache, fever, chills and myalgia may also be seen. Severe dehydration can occur in infants and the elderly. In many cases, the symptoms resolve spontaneously in 1 to 7 days. Deaths are rare except in very young, very old, debilitated or immunocompromised persons. Reiter's syndrome may be a sequela in some cases of gastroenteritis. This syndrome is characterized by mild to severe arthritis, nonbacterial urethritis or cervicitis, conjunctivitis and small, painless, superficial mucocutaneous ulcers. Reiter's syndrome occurs in approximately 2% of cases of salmonellosis.

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Clinical Signs: Enteric Fever

- Systemic salmonellosis
- Caused by *S. typhi* or other species
- Clinical signs
  - Non-specific
  - Gastrointestinal disease
  - Fever, anorexia, headache, lethargy, myalgias, constipation
- Can be fatal: meningitis, septicemia

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Enteric fevers are a severe form of systemic salmonellosis. Although most cases are caused by *S. typhi*, a human pathogen, other species can also cause this syndrome. Gastrointestinal disease may be the first sign, but it usually resolves before the systemic signs appear. The symptoms of enteric fever are non-specific and may include fever, anorexia, headache, lethargy, myalgias and constipation. This disease can be fatal, due to meningitis or septicemia, if not treated quickly.

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Diagnosis

- Isolate organism from feces or blood
- Grows on wide variety of media
  - Enrichment
- Biochemical tests
  - Antigens
  - Phage typing
- PCR

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Salmonellosis can be confirmed by isolating the organisms from feces or, in cases of disseminated disease, from the blood. *Salmonella* will grow on a wide variety of selective and non-selective media. Enrichment broths can increase the probability of isolating the organism. *Salmonella* spp. are identified with biochemical tests, and the serovar can be identified using serology for the somatic (O), flagellar (H) and capsular (Vi) antigens. PCR and other genetic techniques may also be available.

[Photo: *Salmonella* colonies. Dr. Danelle Bickett-Weddle, CFPSH]

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Treatment in Humans

- Antibiotics
  - Ampicillin, amoxicillin, gentamicin, TMS, fluoroquinolones
- Treatment indications
  - Septicemia, enteric fever
  - Elderly, infants, immunosuppressed
- Healthy persons recover 2 to 7 days without antibiotics

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Salmonellosis in humans can be treated with a number of antibiotics including ampicillin, amoxicillin, gentamicin, trimethoprim/sulfamethoxazole and fluoroquinolones. Many isolates are resistant to one or more antibiotics, and the choice of drugs should, if possible, be based on susceptibility testing. Antibiotics are used mainly for septicemia, enteric fever or focal extraintestinal infections. Focal infections may require surgery and prolonged courses of antibiotics. In the elderly, infants and immunosuppressed persons, who are prone to septicemia and complications, antibiotics may be given for gastroenteritis. However most healthy people recover spontaneously in 2 to 7 days and may not require antibiotic treatment. Antibiotics do not usually shorten this form of the disease. They also prolong the period of bacterial shedding and increase the development of antibiotic-resistant strains. Symptomatic treatment of dehydration, nausea and vomiting may be required.

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Non-Typhoidal Salmonellosis and Animals

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Disease in Animals

- Found in all species
  - Mammals
  - Bird
  - Reptiles
  - Amphibians
  - Fish
  - Invertebrates
- Some serovars have narrow host range

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Salmonella spp. have been found in all species of mammals, birds, reptiles, and amphibians that have been investigated. Fish and invertebrates can also be infected. Infections are particularly prevalent in poultry, swine, and reptiles. All species seem to be susceptible to salmonellosis under the right conditions but clinical disease is more common in some animals than others. Some serovars have a narrow host range. Clinical cases are common in cattle, pigs, and horses but are relatively uncommon in cats and dogs.

[Photo: Chicks. USDA, ARS, Keith Weller]

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Disease in Animals

- Incubation period: highly variable
- Infections become symptomatic under stressful conditions
  - Transport
  - Crowding
  - Weaning
  - Parturition
  - Exposure to cold
  - Concurrent diseases

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The incubation period in animals is highly variable. In many cases, infections become symptomatic only when the animal is stressed. Clinical disease usually appears when animals are stressed by factors such as transportation, crowding, food deprivation, weaning, parturition, exposure to cold, a concurrent viral or parasitic disease, sudden change of feed, or overfeeding following a fast. The clinical signs vary with the infecting dose, health of the host, *Salmonella* serovar and strain, and other factors.

[Photo: Pigs in transit. USDA ARS, Scott Baur]

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Clinical Disease: Reptiles

- Clinical disease uncommon
- Syndromes reported
  - Subcutaneous abscesses
  - Septicemia
  - Osteomyelitis
  - Osteoarthritis

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Clinical disease seems to be uncommon in reptiles. Syndromes that have been reported include septicemia (characterized by anorexia, listlessness and death), osteomyelitis, osteoarthritis and subcutaneous abscesses. Progressive, fatal bone infections have been seen in snakes. In one group of free-living turtles, the symptoms included emaciation, lesions of the plastron, a discolored carapace and intestinal, respiratory and hepatic lesions. *Salmonella* spp. have also been implicated in sporadic deaths among tortoises in zoos.

[Photo : Turtle (*Graptemys nigrinoda*) hatchlings. Wikimedia Commons]

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Acute Enteritis: Ruminants, Pigs, Horses

- Diarrhea (watery to pasty)
- Dehydration
- Depression
- Abdominal pain
- Anorexia
- Fever
- Decreased milk production
- Death from dehydration, toxemia

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Acute enteritis is the most common form of salmonellosis in adult animals, and in calves over a week old. This form is characterized by profuse diarrhea, dehydration, depression, abdominal pain and anorexia. The feces are watery to pasty, often foul smelling, and may contain mucus, pieces of mucous membrane, casts, or blood. A fever occurs early in the infection, but can disappear by the time diarrhea develops. In dairy cows, milk production drops acutely. Intestinal salmonellosis usually lasts for 2 to 7 days. Death can occur as the result of dehydration and toxemia. Horses, in particular, often have sever enteritis and may die within 24 to 48 hours. Recovery can be slow.

[Photo: Sick dairy cow. CFSPH]

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Enteritis: Ruminants, Pigs, Horses

- Subacute
  - Adults
  - Diarrhea
  - Weight loss
- Chronic
  - Adults, older calves, growing pigs
  - Emaciation, fever, inappetence, scant feces

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Subacute enteritis may be seen in adult horses, cattle, and sheep. The most obvious symptoms are persistent soft feces, or diarrhea, and weight loss. There may also be mild fever, inappetence, and some dehydration. Chronic enteritis is mainly seen in older calves, adult cattle and growing pigs. The symptoms can include progressive emaciation (see photo of emaciated horse), low-grade intermittent fever and inappetence. The feces are usually scant and may be normal or contain mucus, casts, or blood. Rectal strictures can be sequelae in growing pigs.

[Photo: Emaciated horse. Cornell College of Veterinary Medicine, Dr. John M. King]

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Septicemia: Ruminants, Horses, Pigs

- Young animals
  - Very young calves
  - Lambs, foals
  - Pigs up to 6 months
- Clinical signs
  - Depression, fever
  - CNS signs or pneumonia (calves, pigs)
  - Dark discoloration of skin (pigs)
- Death 1 to 2 days

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Septicemia is the most common syndrome in very young calves, lambs and foals, and in pigs up to 6 months of age. The symptoms include marked depression, high fever and often, death within 1 to 2 days. Diarrhea can occur in some animals. Central nervous system (CNS) signs or pneumonia may be seen in calves and pigs. Pigs may also develop a dark reddish or purple discoloration of the skin, particularly on the ears and ventral abdomen.

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Other Signs: Ruminants, Horses, Pigs

- Abortion
  - Associated serovars
    - Dublin (cattle)
    - Abortusovis (sheep)
    - Abortusequi (horses)
  - May be first clinical sign in cows with subacute enteritis
- Joint infections/gangrene

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Pregnant animals may abort, either with or without other clinical signs. Serovars often associated with abortions include *Salmonella* Dublin in cattle, *Salmonella* Abortusovis in sheep and *Salmonella* ser. Abortusequi in horses. In cows with subacute enteritis, the first symptom may be abortion, followed after several days by diarrhea. Abortions in pregnant ewes may be followed by fetid, dark red vaginal discharge and sometimes death. Another sign seen in calves are joint infections or gangrene at the limb extremities (see photo), tips of the ears and tail.

[Photo: Gangrene limb of calf. Cornell College of Veterinary Medicine, Dr. John M. King]

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Clinical Signs: Dogs and Cats

- Acute diarrhea
  - Recover 3 to 4 weeks
- Septicemia
- Cats
  - Chronic febrile illness
- Abortion
- Birth of weak offspring

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In dogs and cats, the most common form is acute diarrhea with or without septicemia. Most cats and dogs with acute diarrhea recover within 3 to 4 weeks. Pneumonia, abscesses, meningitis, osteomyelitis, cellulitis or conjunctivitis may also be seen. A chronic febrile illness characterized by anorexia and lethargy, but no diarrhea, has been reported in cats. Pregnant dogs and cats may abort or give birth to weak puppies or kittens.

[Photo: Veterinarian examining cat. Dr. Danelle Bickett-Weddle, CFSPH]

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Clinical Signs: Birds

- Very young birds
- Anorexia
- Lethargy
- Diarrhea
- Increased thirst
- CNS signs

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Most clinical cases are seen in very young birds. The symptoms may include anorexia, lethargy, diarrhea, increased thirst and CNS signs.

[Photo: Chicks in a basket. Steve Roney, USDA]

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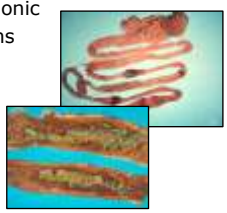
Post Mortem Lesions

- Not pathognomonic
- Intestinal lesions most common
  - Lower ileum
  - Large intestine



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The necropsy lesions are not pathognomonic. They may include necrotizing fibrinous enteritis (top photo), lesions associated with septicemia, or both. Intestinal lesions are most common and severe in the lower ileum and large intestine. In acute enteritis, there is extensive hemorrhagic enteritis, with mucosal erosions and often whole blood in the lumen (bottom photo). Similar lesions may be found in the abomasum. The mesenteric lymph nodes are usually edematous and hemorrhagic, and there may be inflammation in the wall of the gall bladder. Other lesions may include fatty degeneration in the liver, bloodstained fluid in the serous cavities, and petechial hemorrhages in the heart and sometimes other organs. In cattle with chronic salmonellosis, the intestinal wall is thickened and discrete areas of necrosis are usually found in the mucosa of the cecum and colon. An inflamed granular surface may be seen under the necrotic regions.

[Photo source: Cornell College of Veterinary Medicine, Dr. John M. King]

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Diagnosis

- Isolate organism from feces or blood
  - Selective and non-selective media
  - Enrichment
  - Biochemical tests
- Serology
  - Herds or flocks
- PCR
- Healthy carriers

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Salmonellosis can be confirmed by isolating the organisms from feces or, in cases of disseminated disease, from the blood. After an abortion, the bacteria may be found in the placenta, vaginal exudate and fetal stomach. *Salmonella* spp. are identified with biochemical tests, and the serovar can be identified by serology for the somatic (O), flagellar (H) and capsular (Vi) antigens. Serology can be useful for diagnosis in a herd or flock. It is also used to identify carriers in poultry *Salmonella* eradication programs. Serologic tests include agglutination tests and enzyme-linked immunosorbent assays (ELISAs). Some ELISAs can be used for bulk milk screening or on freeze thawed muscle tissue samples (tissue fluid) from pigs. Most serologic tests detect a limited number of serovars or serogroups. Serology is of limited use in individual animals, as antibodies do not appear until two weeks after infection, and antibodies may also be present in uninfected animals. Polymerase chain reaction (PCR) and other genetic

techniques may also be available. Diagnosis of clinical cases and identification of carriers is complicated because *Salmonella* spp. can be found in healthy carriers.

[Photo: Researcher testing eggs for *Salmonella* . USDA ARS]

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Treatment

- Antibiotics
  - Septicemia
  - Not recommended for enteric disease
    - May affect intestinal flora and increase emergence of resistant strains
- Fluid replacement
- NSAIDs
  - Endotoxemia

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Septicemic salmonellosis can be treated with a number of antibiotics including ampicillin, amoxicillin, gentamicin, trimethoprim/sulfamethoxazole, third generation cephalosporins, chloramphenicol and fluoroquinolones. Many isolates are resistant to one or more antibiotics, and the choice of drugs should, if possible, be based on susceptibility testing. Antibiotics can favor the persistence of *Salmonella* spp. in the intestines after recovery, affect the intestinal flora, and increase the emergence of antibiotic-resistant strains. For these reasons, antibiotics might not be used for enteric disease. Fluid replacement, correction of electrolyte imbalances and other supportive care is important in cases of enteritis. Nonsteroidal anti-inflammatory drugs may be given to decrease the effects of endotoxemia. Antibodies to *Salmonella* lipopolysaccharide may also be used in some cases.

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Prevention and Control

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Prevention in Humans

- Food-borne diseases
  - Avoid raw or undercooked eggs, poultry, meat; unpasteurized milk/dairy
  - Wash foods before eating
  - Avoid cross-contamination of food
    - Keep uncooked and cooked foods
    - Wash hands and kitchen tools
  - Do not feed infants or change diapers while handling food

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To decrease the risk of salmonellosis, both food safety practices and the prevention of transmission from animals are important. To reduce the risk of food-borne disease: 1) Raw or undercooked eggs, poultry and other meats should be avoided. 2) All meat should be cooked until it is no longer pink in the middle. 3) Unpasteurized milk and other unpasteurized dairy products should not be drunk or eaten. 4) Raw vegetables should be thoroughly washed before eating. 5) Cross-contamination of foods should be prevented. 6) Uncooked meats should be kept separate from produce, cooked and read-to-eat foods. The hands and any kitchen tools that contact uncooked foods should be thoroughly washed after handling potentially contaminated foods. The hands should also be washed before handling foods. 7) Infants should not be fed or have their diapers changed while the caregiver is working with raw meats or eggs.

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Prevention in Humans

- Animal contact
  - Wash hands after contact
  - If immunocompromised, avoid contact with reptiles, young chicks, ducklings
  - Reptiles
    - Children under 10 years of age
    - Wash hands, cages, and surfaces
    - Change clothes
    - Supervision
    - Do not allow reptiles to roam freely

To reduce the risk of acquiring salmonellosis from animals: 1) The hands should always be washed with hot, soapy water, immediately after contact with any animal feces. 2) People who are immunocompromised should avoid contact with reptiles, young chicks and ducklings. 3) They should also be particularly cautious when visiting farms or petting zoos. Other zoonosis prevention recommendations for those who are immunocompromised can be found on the CDC web site. Extra precautions should be taken with reptiles, as many seem to shed *Salmonella* spp. Children under 10 seem to be particularly susceptible to severe salmonellosis after contact with reptiles. No human vaccines to prevent zoonotic or foodborne salmonellosis exist.

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Prevention in Animals

- Herds and flocks
  - Buy from *Salmonella*-free sources
  - Isolate new animals
  - All in/all out
- Outbreak
  - Identify carriers
    - Isolate, treat, or cull
  - Retest treated animals
  - Clean and disinfect

The risk of introducing salmonellosis into a herd/flock can be decreased by buying animals or eggs from *Salmonella*-free sources, isolating newly acquired animals, and practicing "all in/all out" herd or flock management, where appropriate. Rodent control is also important. Feed and water sources should be *Salmonella*- free. During a herd outbreak, carrier animals should be identified and either isolated and treated, or culled. Treated animals must be re-tested several times to ensure that they no longer carry *Salmonella.* Fecal contamination of feed and water supplies should be prevented. Contaminated buildings and equipment should be cleaned and disinfected, and contaminated material should be disposed of.

[Photo: Isolated beef cow. CFPSH]

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Prevention in Animals

- Preventing clinical disease
  - Good hygiene
  - Minimize stressful events
  - Colostrum
  - Vaccination
    - Also reduces colonization and shedding
- All reptiles are a source
  - Do not treat to eliminate

Clinical salmonellosis can be decreased by good hygiene and minimizing stressful events. Colostrum is important in preventing disease in young animals. Vaccines are available for some serovars such as *Salmonella* Dublin, *Salmonella* Typhimurium, *Salmonella* Abortusequi *and Salmonella* Choleraesuis in some countries. Vaccines can reduce the level of colonization and shedding of *Salmonella* spp. into the environment, as well as clinical disease. Competitive exclusion by administration of *Salmonella* free cultures of fecal organisms may be used in young birds. All reptiles should be considered to be potential sources of *Salmonella.* The Association of Reptile and Amphibian Veterinarians (ARAV) discourages veterinarians from treating reptiles with antibiotics to eliminate Salmonella, as this has not been effective in the past and may increase the development of antibiotic-resistant strains of bacteria.

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Additional Resources

- World Organization for Animal Health (OIE)
  - www.oie.int
- U.S. Department of Agriculture (USDA)
  - www.aphis.usda.gov
- Centers for Disease Control and Prevention (CDC)
  - http://www.cdc.gov/salmonella/
- Center for Food Security and Public Health
  - www.cfsph.iastate.edu

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Acknowledgments

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