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Searching for Salmonella

Background

Salmonella species are responsible for two distinct syndromes. Nontyphoidal *Salmonella* are common causes of food borne gastroenteritis. Typhoidal *Salmonella* cause enteric fever; an important differential diagnosis in any traveller returning from a tropical country with fever.

Objective

This article describes the spectrum of disease that occurs with Salmonellosis infections and particular subgroups of patients who are more susceptible to severe disease. An appreciation of this will allow the clinician to manage these infections appropriately.

Discussion

Nontyphoidal Salmonellosis infections causing gastroenteritis are common in our community. Infection is caused by ingesting contaminated food or water, or occasionally by contact with an infected person. Most cases are self limiting and the focus of management is effective rehydration. Antibiotic therapy is seldom warranted but important exceptions exist including neonates, the immunocompromised, and in particular circumstances, the elderly. Enteric fever always warrants antibiotic treatment. Notification to the appropriate health authority assists with investigating possible outbreaks.

■ ***Salmonella* species are motile Gram negative bacilli responsible for a range of clinical manifestations in humans. The most common of these is gastroenteritis. Infections are caused by contact with contaminated food or water, or less commonly, after contact with an infected individual.**

There are over 2000 serotypes of *Salmonella* species described, however a relatively small number are important pathogens in humans.¹ It is important to distinguish between:

- *Salmonella* serotypes causing enteric fever, and
- 'nontyphoidal *Salmonella*' serotypes (*Table 1*).

The causative organisms of enteric fever are *S. Typhi* and *S. Paratyphi* A, B and C. These are acquired after ingesting food or water contaminated with the bacteria. These serotypes are not endemic in Australia and enteric fever occurs almost exclusively in tropical and developing countries with poor standards of hygiene. Cases in Australia occur in returned travellers. The syndrome is marked by fever and abdominal symptoms, with a high rate of complications and mortality if untreated.

Many other nontyphoidal serotypes cause the remainder of clinical disease, such as gastroenteritis; these vary according to geographic location. In Australia the most common serotype is *S. Typhimurium*.²

The natural habitat for nontyphoidal *Salmonella* species is farm and pet animals, in particular, poultry and eggs.¹ Ingesting raw or undercooked food or cooked food that is cross contaminated may lead to human infection. The incidence of Salmonellosis infections in developed countries has increased in recent years. In the United States, *Salmonella* is the most commonly isolated pathogen causing food borne illness;¹ in Australia it is second after *Campylobacter pylori*.² Notifications of *Salmonella* across Australia increased by 5% in 2006 compared to historical figures.² This global trend may be due to the increased manufacturing of processed food and the popularity of ready to eat food. Several large outbreaks in Australia may account for some of the increase in notifications. The largest of



these was the *S. Typhimurium* outbreak in Tasmania in 2005, associated with the consumption of raw or undercooked eggs and the multistate *S. Saintpaul* outbreak associated with rockmelons in 2006.^{2,3} *S. Enteritidis* (Figure 1) is a serotype of particular concern as this is passed vertically from the oviducts of infected chickens to the egg during development. This strain is not endemic in Australia, however large outbreaks overseas have been associated with undercooked eggs.²

Prevention of infection

Prevention of Salmonellosis infection is achieved by:

- attention to personal hygiene, particularly after toileting and before preparing food
- avoiding raw or undercooked meat, poultry or eggs
- cooking an egg until the yolk is solid (kills all bacteria)
- washing raw fruit and vegetables before preparation and eating, and
- avoiding contaminating cooked food with utensils used to prepare raw food such as knives or chopping boards.

Clinical features

Infections caused by *Salmonella* cause distinct clinical syndromes. These include:

- gastroenteritis
- enteric fever
- bacteraemia
- extra-intestinal localised infection, eg. osteomyelitis, endovascular infection or focal abscess
- asymptomatic chronic carrier state.

Gastroenteritis

Gastroenteritis is the most common manifestation of infection with nontyphoidal *Salmonella*. Gastroenteritis caused by *Salmonella* is often clinically indistinguishable from that caused by other pathogens (Table 2). Many patients have mild or asymptomatic disease. Symptoms usually begin 24–48 hours (range 8–72 hours) after ingestion of contaminated food or water, with fever, headache, abdominal cramps and diarrhoea.¹ Vomiting does not always occur. Stools are usually loose and moderate in volume. The severity of the illness and the time to symptom onset are related to the amount of bacteria ingested (infectious dose).⁶ Diarrhoea is usually self limiting, lasting 3–7 days. Diarrhoea lasting more than 10 days or fever lasting more than 72 hours suggests an alternate diagnosis.¹

Gastroenteritis is complicated by *Salmonella* bacteraemia in less than 5% of cases.⁷ This is usually self limiting, however, the risk of endovascular infection increases with age and is estimated to be 10% in those aged over 50 years.⁸ Complications of bacteraemia include endocarditis, mycotic aneurysms and osteomyelitis. In a patient with persistent fever beyond 72 hours, or systemic symptoms such as chills or rigors, consideration should be made to further investigate for complications.

Host factors associated with increased susceptibility to Salmonellosis infection are outlined in Table 3. These predisposing factors may result in:

Table 1. *Salmonella* serotypes and the clinical syndromes they produce

Organism	Syndrome
Typhoidal <i>Salmonella</i> <ul style="list-style-type: none"> • <i>S. Typhi</i>, <i>S. Paratyphi</i> A, B, C 	Enteric fever (typhoid and paratyphoid fever) Chronic carrier state
Nontyphoidal <i>Salmonella</i> <ul style="list-style-type: none"> • Numerous serotypes (eg. <i>S. Typhimurium</i>, <i>S. Enteritidis</i>, <i>S. Saintpaul</i>) 	Gastroenteritis Bacteraemia Focal infections

Figure 1. *Salmonella* Enteritidis on XLD agar



Photo courtesy Dorothy I Slater

- an increased likelihood of symptomatic infection
- more severe infection, or
- more serious complications such as bacteraemia, metastatic infection or prolonged illness.

Enteric fever

Enteric fever is caused by the serotypes *S. Typhi* and *S. Paratyphi* A, B and C, producing clinical syndromes commonly referred to as typhoid and paratyphoid fever, respectively. These are exclusively human pathogens, compared to nontyphoidal *Salmonella* where animals are involved. The syndrome is characterised by fever and abdominal symptoms, with an incubation period most commonly 10–14 days (range 3–21 days).¹ Clinical symptoms are highly variable, and enteric fever should be considered in any patient returning from an endemic country with a fever.

After a prodrome of systemic symptoms including chills, diaphoresis, malaise, headache, dry cough, myalgia and arthralgia, the development of a progressive 'step wise' fever follows, classically rising daily. A faint rash of small erythematous maculopapular lesions (rose spots) appears in approximately 20% of patients; most easily seen in the fair skinned. Liver involvement is common, with raised liver function tests, particularly bilirubin and alanine aminotransferase, which may produce clinical jaundice. Abdominal symptoms are common including pain, and constipation is more common than diarrhoea. Severe complications include intestinal bleeding or perforation.



Diagnosis

Nontyphoidal Salmonella

The issue of when to order a faecal specimen is frequently encountered in general practice. Salmonella can be readily isolated from the stool of an infected person. Many patients will have a self limiting course and intervention is not necessary. Accurate diagnosis may provide prognostic information but is generally not required.

Faecal microscopy is recommended in patients with severe symptoms, recent overseas travel, recurrent or persisting diarrhoea, or in the immunocompromised (Table 4).^{10,11}

It has been common practice to request stool specimens on two consecutive days to increase the diagnostic yield. However, recent studies have demonstrated that a single specimen is sufficient when investigating for bacterial pathogens (Table 4).^{12,13} A formed specimen should not be sent; instruct the patient to wait until they have a loose motion. There is value in examining more specimens when investigating for parasitic infections (eg. chronic diarrhoea); two specimens collected at different times should be requested. The turnaround time for a result is 48–72 hours and may be expedited if accurate clinical notes are provided to the laboratory, indicating a suspicion of bacterial infection. Antibiotic susceptibility testing is not routinely performed for nontyphoidal

Salmonella isolates. Reference laboratories perform resistance surveillance and this information helps to direct guidelines. If susceptibility data is required, discuss this with your relevant microbiology laboratory.

Blood cultures should be considered if fever persists beyond 72 hours.

Enteric fever

The diagnosis of enteric fever requires the isolation of *S. Typhi* or *S. Paratyphi* from blood, faeces or urine. Often multiple specimens are required as the sensitivity of a single specimen is low. In certain cases a bone marrow aspirate and culture is required, which has the highest sensitivity. Serology is available but generally not recommended due to problems with low sensitivity and specificity. There are other important differential diagnoses in a returned traveller with fever. A suspicion of enteric fever usually warrants referral to hospital for inpatient investigation.

Management

For nontyphoidal Salmonella, the primary aim in both children and adults is to provide adequate oral rehydration. In certain circumstances nasogastric hydration or intravenous fluid therapy is warranted, as determined by clinical judgment. Antimotility agents are generally

Table 2. Differential diagnosis of community acquired infectious diarrhoea

Organism	Children (<6 years of age) ⁴	Adults ⁵	Food borne illness ²
Viral	Most common overall	Common	Rare
<ul style="list-style-type: none"> • Rotavirus • Norovirus[#] • Adenoviruses • Astroviruses 	+++ ++ + +	(uncommon) +++ +	
Bacteria	Uncommon	Common	Most common
<ul style="list-style-type: none"> • <i>Campylobacter pylori</i> • Nontyphoidal Salmonella • <i>Shigella</i> species • Pathogenic <i>Escherichia coli</i> 		Pathogenic <i>E. coli</i> most common cause in returned traveller Most common cause in hospitalised patient	<ul style="list-style-type: none"> • <i>Campylobacter pylori</i> • Nontyphoidal Salmonella • <i>Shigella</i> species • Listeria • Vibrio • Typhoidal Salmonella
<ul style="list-style-type: none"> • Antibiotic associated <i>Clostridium difficile</i>* 			Nil
Parasites	Unusual	Least common	
<ul style="list-style-type: none"> • <i>Giardia intestinalis</i> • <i>Cryptosporidium parvum</i> • <i>Entamoeba histolytica</i> 	Giardia and cryptosporidium associated with patient being in day care	Consider if prolonged symptoms or travel associated	Associated with contaminated water

Note: This table provides a guide to the most commonly isolated pathogens. Significant seasonal variation exists, with viral pathogens predominating in winter and bacterial pathogens in warmer months

[#] Norovirus is the major cause of community and hospital associated gastroenteritis outbreaks. In one study it was found to be the most common cause of community acquired gastroenteritis in adults, followed by bacterial pathogens (as listed above), adenovirus, giardia and cryptosporidium⁵

* Testing for *C. difficile* requires a specific request and should be included if antibiotics have been used in past 6 weeks



advised against, and should not be used in children, due to concerns of prolonging bacterial excretion and serious side effects such as ileus, coma and death.¹⁰

Antibiotics have a limited role in the treatment of infectious diarrhoea (Table 5). Most causes including bacterial diarrhoea are self limiting. Viral pathogens do not require antibiotics and the excretion of bacteria may be prolonged after antibiotic therapy. A meta-analysis of antimicrobial therapy for Salmonella gastroenteritis found no benefit in terms of duration of symptoms or fever.¹⁴

The management of enteric fever usually requires hospitalisation, close monitoring for complications and a course of intravenous antibiotics. This is followed by oral antibiotics if the organism is susceptible to suitable agents. Antibiotic resistance in typhoidal

Salmonella is a major public health concern worldwide, and we are seeing many resistant strains in returned travellers, especially from the Indian subcontinent.

Public health implications

Infections caused by Salmonella are required to be notified to state or territory health departments by the laboratory, and in most states, by the treating clinician (check with your state health department). All strains of Salmonella are typed by various methods (serotyping, phage typing and susceptibility patterns) to provide ongoing surveillance for the emergence of new strains in the community and to investigate linked cases. This information helps in the formulation of prevention strategies.

The decision to conduct an investigation is based on several factors: if cases are clustered in time, to a specific geographic location, or are proven by molecular methods to be the same strain. The purpose of an investigation is to determine if there is an outbreak, and if so, to locate the common source. This takes the form of detailed interviews and questionnaires of affected people. Important points include date of onset, symptoms, travel history, occupation, and a detailed history of food consumed and where it was obtained. If a food source is implicated the health authority will often conduct environmental sampling (eg. food, equipment) and initiate control measures. Occasionally cohort studies will be performed to look for an association with a particular common food source.¹⁶

A common scenario is a general practitioner recognising a similar illness in multiple members of the same family or community. If Salmonella is isolated from one member, it is likely that other members of the family are infected with the same organism; especially if there is a common food source. Prompt notification to a health authority can expedite appropriate investigations. Patients should be instructed to keep any remaining portion of suspicious food in the refrigerator until it can be collected by an environmental health officer.

All patients with Salmonellosis infection should be educated about correct personal hygiene, especially after toileting and before preparing food. They should not prepare food for others. For nontyphoidal Salmonellosis infections, patients are informed not to return to work until diarrhoea has resolved. Of particular importance is any person working in an industry where contamination of food or person-to-person spread is a possibility. This includes food handlers, child care workers and health care workers. The state or territory health department will advise when it is safe for the worker to return to work.¹⁶ For all patients with enteric fever (typhoidal Salmonella), the responsible health department will conduct follow up after recovery of the clinical illness. Three consecutive weekly faecal specimens are requested to look for carriage of the organism.

Summary of important points

- Salmonellosis infections are acquired by ingesting contaminated food or water.

Table 3. Host factors associated with susceptibility to Salmonellosis infection⁹

Age
Neonates and the elderly
Cell mediated immunity
HIV
Immunosuppression (eg. organ transplantation or corticosteroid therapy)
Phagocytic function
Haemoglobinopathies (eg. thalassaemia, sickle cell anaemia)
Gastric acidity
Antacid medication
Achlorhydria
Altered intestinal flora
Antimicrobial therapy
Bowel surgery
Mucosal integrity
Inflammatory bowel disease
Gastrointestinal malignancy

Table 4. Faecal microscopy in patients with diarrhoea

- Faecal microscopy is indicated in the following situations:
 - severe symptoms suggestive of bacterial invasion, such as bloody diarrhoea, severe abdominal pain, rigors or prolonged fever
 - other epidemiological factors such as recent travel or contact with another person with gastroenteritis
 - recurrent or persistent diarrhoea; may indicate an unusual pathogen and faecal samples will guide therapy
 - immunocompromised patients; including HIV, transplant, recent chemotherapy
- Stool samples
 - send only loose motions, not solid samples
 - only a single sample required for a suspected bacterial cause
 - indicate on the request form that a bacterial cause is suspected
 - send two specimens taken at different times for suspected parasitic infection



Table 5. Management of nontyphoidal Salmonellosis infections – recommendations according to patient population

Patient group	Recommendations	Comments
• Uncomplicated gastroenteritis	Supportive management, no antibiotics	Potential risks outweigh benefits
• Severe gastroenteritis requiring hospitalisation	Consider antibiotics	Aim to shorten illness and prevent complications
• Severe pain or diarrhoea		
• High fever, rigors		
• Suspected or proven bacteraemia		
• Suspected complication	Consider antibiotics	Look for alternate diagnosis
• Fever >72 hours		
• Age <2 years	Consider antibiotics	Treat neonates <3 months of age (at risk of complications, eg. meningitis and higher mortality ¹⁰)
• Age >50 years	Consider antibiotics	Especially if known atherosclerotic disease, endovascular graft/stent or joint prosthesis ¹⁵
• Immunocompromised	Treat with antibiotics – prolonged course (eg. 14 days) and close follow up	Treat while awaiting culture confirmation

Note. Empiric treatment is ciprofloxacin 500 mg bd for 5–7 days or azithromycin 1 g followed by 500 mg for 6 days (7 days total). If oral therapy cannot be tolerated, use ceftriaxone 2 g IV daily until a switch can be made to one of the above oral medications.¹⁰ There is increasing resistance in *Salmonella* to many first line antimicrobials (especially ciprofloxacin), particularly in isolates from Asia. For patients with a recent travel history, azithromycin is the preferred first line option

- Gastroenteritis caused by *Salmonella* is clinically indistinguishable from that caused by other pathogens.
- Most cases are self limited and antibiotic therapy is not warranted.
- Patients with Salmonellosis infection should not prepare food for others and should be excluded from work until the diarrhoea resolves. For food handlers, child and health care workers, a state or territory health department will advise when it is safe to return to work.
- In severe disease (bloody diarrhoea, severe pain, rigors, and prolonged fever) faecal microscopy should be requested and empirical treatment considered.
- Antibiotic treatment should be considered for young children (<2 years) and the elderly, particularly those with atherosclerotic disease and prostheses, and should be given to immunocompromised patients.
- Uncommon complications of nontyphoidal *Salmonella* related bacteraemia are endocarditis, mycotic aneurysms and osteomyelitis.
- Enteric fever is a specific syndrome caused by *S. Typhi* and *S. Paratyphi*. Antibiotic treatment is always required, generally requiring hospital admission.
- Symptoms of enteric fever are highly variable, and enteric fever should be considered for any patient returning from an endemic country with a fever.
- Prompt notification to an appropriate health authority may expedite an investigation and help to prevent subsequent cases. (Notification is mandatory in most states of Australia.)

Resources

Patient fact sheets. Available at:

- www.health.vic.gov.au/ideas/diseases/gas_dsai
- www.health.nsw.gov.au/factsheets/infectious/salmonellosis.

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