Salmonellosis

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1404

Salmonella

1- *Typhoid / paratyphoid*

2- *Non typhoidal (NTS)*

- *Salmonella* Typhi and *Salmonella* Paratyphi A, B, and C
- gram-negative bacilli, species *S. enterica* subspecies *enterica*
- categorized serologically by O (O polysaccharide) and H (flagellar) antigens.

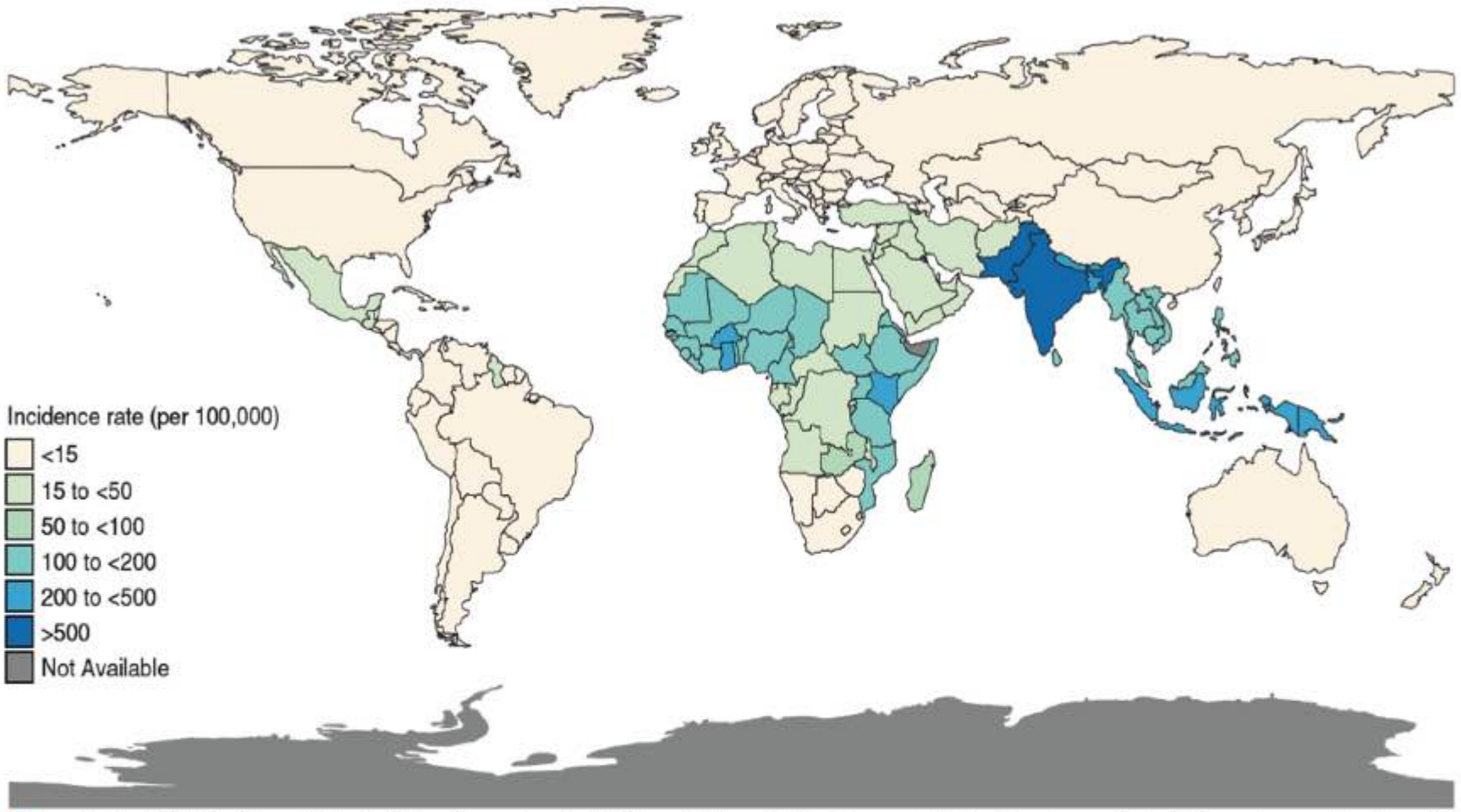

FIG. 102.1 Global distribution of typhoid and paratyphoid fever. Estimated incidence of typhoid and paratyphoid fever by country from the Global Burden of Disease Study 2019. *(Source: Institute for Health Metrics and Evaluation. Used with permission. All rights reserved.)* Map lines delineate study areas and do not necessarily depict accepted national boundaries.

Epidemiology

Natural course

- Preantibiotic era: 10-15% fatal (resolved over a 3- to 4-week)
- current mortality: 0.5-1%

Source of Infection

- S.Typhi, Paratyphi A, B: stool of infected humans
- S.Paratyphi C: humans and animals

Transmission:

- ingestion (fecally contaminated **water** or food)
- person-to-person transmission (less common)

Relapse

- up to 10% of untreated cases
- within 2 weeks after initial resolution of fever
- same strain
- milder symptoms
- same antibiotic susceptibility

chronic asymptomatic carriage: shedding of the bacteria in stool or urine for more than a year

- preantibiotic era: up to 5% , gallbladder disease being the major risk factor , greater in adults (3%–10%) than in young children (<1%)
- Urinary carriage: urinary schistosomiasis
- gallbladder(biofilms on cholesterol gallstones)
- association between chronic carriage and risk of gallbladder carcinoma

TABLE 100.2 Clinical Features of Typhoid and Paratyphoid Fever

	CLINICAL FEATURE	APPROXIMATE FREQUENCY[a]
Flulike symptoms	Fever	>95%
	Headache	80%
	Chills	40%
	Cough	30%
	Myalgia	20%
	Arthralgia	<5%
Abdominal symptoms	Anorexia	50%
	Abdominal pain	30%
	Diarrhea	20%
	Constipation	20%
Physical findings	Coated tongue	50%
	Hepatomegaly	10%
	Splenomegaly	10%
	Abdominal tenderness	5%
	Rash	<5%
	Generalized adenopathy	<5%

[a]The proportion of patients demonstrating these clinical features of enteric fever varies, depending on the time, the region, and the type of clinical population (hospitalized or ambulatory) assessed. Estimates are drawn from recent case series in an endemic area, with patients presenting for ambulatory or inpatient care.[92,96]
Modified from Magill AJ, Ryan ET, Hill DR, Solomon T, eds. Hunter's Tropical Medicine and Emerging Infectious Diseases. *9th ed. Philadelphia: Saunders; 2013:568–576.*

- relative bradycardia (pulse-temperature dissociation)
- Rose spots
- A white or yellowish brown coating of the tongue that spares the tongue's edges

TABLE 100.3 Complications of Typhoid and Paratyphoid Fever

SYSTEM	COMPLICATION	NOTES
Gastrointestinal	Hemorrhage	10%–15% in hospitalized patients
	Perforation	3% in hospitalized patients
Hepatobiliary	Jaundice	1%–3% in hospitalized patients
	Hepatitis	Usually subclinical (↑ ALT/AST)
	Acute cholecystitis	Rare; gallbladder may perforate
Neurologic	Mild encephalopathy	Confusion or apathy common
	Severe encephalopathy	Delirium, stupor, or coma
	Seizures	Common in children ≤5 yr
	Meningitis	Rare, primarily infants
	Guillain-Barré syndrome	Reported
Respiratory	Bronchitis	Dry cough is common
	Pneumonia	May be other concomitant bacterial infection (e.g., *Streptococcus pneumoniae*)
	Empyema	Rare reports
Cardiovascular	Myocarditis	Usually subclinical (ECG changes)
	Endocarditis	Rare reports
Hematologic	Anemia	Usually subclinical
	Disseminated intravascular coagulation	Usually subclinical (↑ PT/PTT)
Other	Musculoskeletal pyogenic infections	Osteomyelitis (particularly vertebral), psoas abscess and others reported
	Hemolytic-uremic syndrome	Reported
	Miscarriage	Reported

Metastatic Pyogenic Complication

- pyogenic abscess formation infrequent (Paratyphi C is more likely to cause abscesses)
- Empyema
- Osteomyelitis
- muscle abscess (particularly involving the psoas)
- endovascular infections , endocarditis

Lab

- Majority not have leukocytosis, neutrophilia, or increased immature neutrophils
- leukocytosis or leukopenia may be present
- Elevated ALT, AST

Diagnosis

Clinical:

- Non endemic: fever> 3 d + exposure to endemic area in last 1-6 w
- Endemic areas: T> 39°C, ill appearance, young age (<5 years), and any abdominal complaints

Culture:

- blood, bone marrow, stool, urine, or other clinical specimen
- Sensitivity (40-80%)(average sensitivity of 61%), prior receipt of antibiotics

Serology: widal

- false-negative(early), false-positive(past infection or previous exposure to cross-reactive antigens or vaccination)
- LDL TUBEX: IgM Ab O:9 Ag
- Thyphidot assay: IgG, IgM
- specificity of the assay (50%-70%)

Molecular Approaches

Chronic Carriage

Management : antibiotics

- Chloramphenicol: bone marrow aplasia in up to 1 in 10,000
- Ampicillin
- Trimethoprim-sulfamethoxazole
- Fluoroquinolones: Lower rates of relapse and carriage compared with those associated with use of chloramphenicol or third-generation cephalosporins
- third-generation cephalosporins
- Azithromycin: lower rates of clinical failure and substantially less relapse than third-generation cephalosporins
- aztreonam

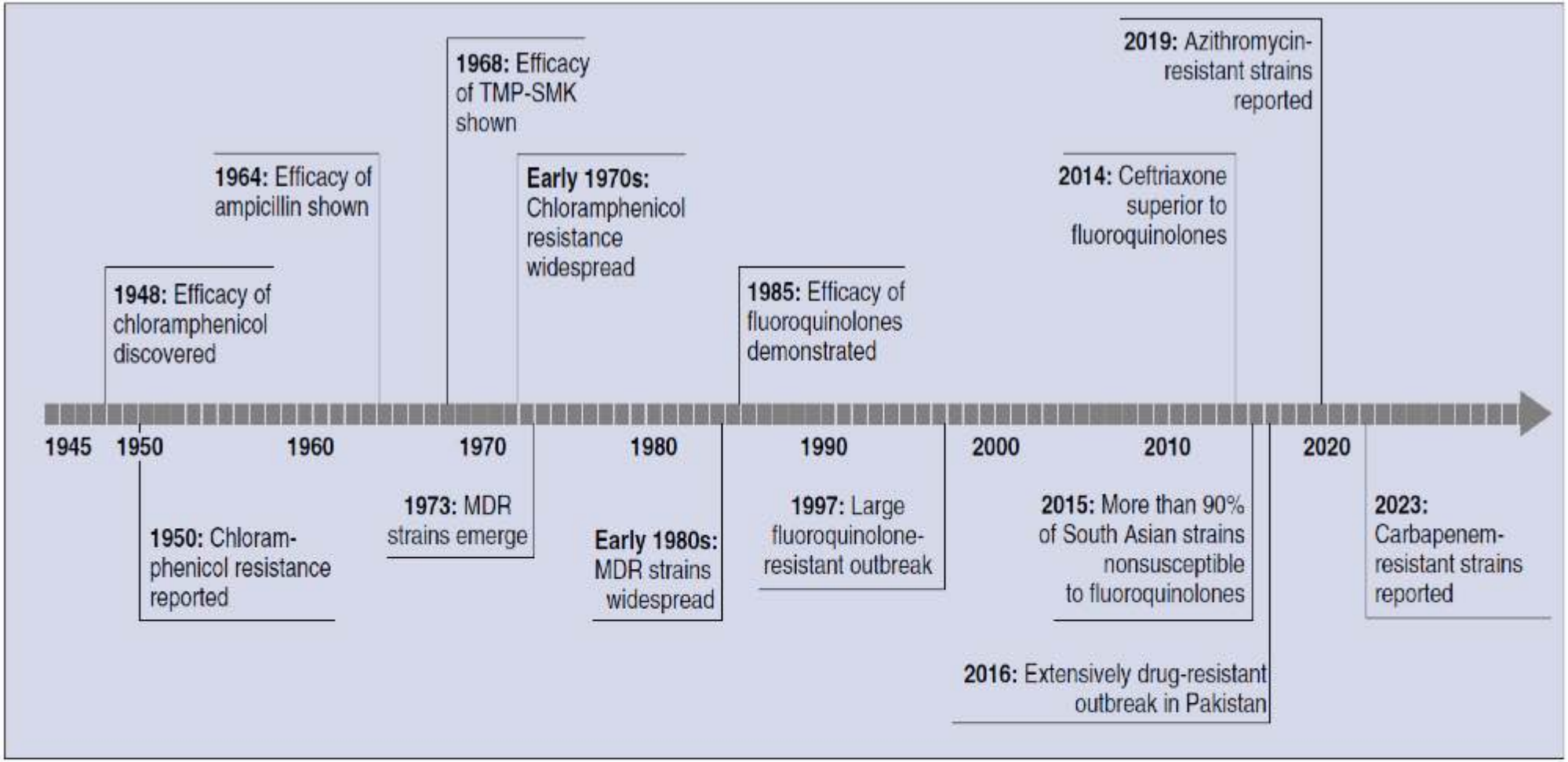

FIG. 102.4 History of antibiotic efficacy studies and the emergence of antimicrobial resistance in *Salmonella* Typhi. *MDR,* Multidrug resistant; *TMP-SMX,* trimethoprim-sulfamethoxazole. *(From Andrews JR, Qamar FN, Charles RC, et al. Extensively drug-resistant typhoid—are conjugate vaccines arriving just in time?* N Engl J Med. *2018:379;1493–1495.)*

TABLE 102.4 Antibiotics Commonly Used in Treating Patients with Enteric Fever

	ANTIBIOTIC	ROUTE	TYPICAL PEDIATRIC DOSAGE[b]	ADULT DOSAGE	TYPICAL DURATION	COMMENTS
Original first-line agents	Chloramphenicol	PO/IV	12.5–25 mg/kg qid	2–3 g/day (divided qid)	14–21 days	These agents are effective for susceptible strains; however, multidrug resistance to all of these agents is common in many areas.
	Amoxicillin	PO	25–35 mg/kg tid	1 g tid	14 days	
	Ampicillin	IV	25–50 mg/kg q6h	2 g q6h	14 days	
	TMP/SMX	PO/IV	8–12 mg/kg/day (TMP) 40–60 mg/kg/day (SMX) (divided qid)	160 mg/800 mg qid	14 days	
Fluoroquinolones	Ofloxacin	PO/IV	15 mg/kg bid	400 mg PO bid	5–14 days	Ofloxacin and ciprofloxacin are effective for nalidixic acid–susceptible strains. Short courses of 5–7 days are acceptable in uncomplicated cases. Ten- to 14-day courses are recommended in patients requiring hospitalization or parenteral therapy. Gatifloxacin appears effective for uncomplicated cases caused by NaR strains.
	Ciprofloxacin	PO/IV	15 mg/kg bid	500 mg PO bid	5–14 days	
	Gatifloxacin	PO	10 mg/kg qd	10 mg/kg/day qd	7 days	
Third-generation cephalosporins	Ceftriaxone	IV	50–100 mg/kg qd	1–2 g IV qd	7–14 days[c]	These are an alternative to fluoroquinolones for strains with decreased fluoroquinolone susceptibility, and for empirical therapy in areas where decreased fluoroquinolone susceptibility is common.
	Cefixime	PO	10 mg/kg bid	200 mg PO bid	7–14 days	
	Aztreonam	IV	50 mg/kg q8h	2g q8h		Alternative to ceftriaxone for cephalosporin-allergic patients.
Macrolides	Azithromycin	PO	20 mg/kg qd	500–1000 mg PO qd	7 days	These are an alternative to fluoroquinolones for strains with decreased fluoroquinolone susceptibility, and for empirical therapy in areas where decreased fluoroquinolone susceptibility is common.
Carbapenems	Meropenem	IV	20–40 mg/kg q8h	1–2 g q8h	10 days	Case series data only (in XDR typhoid); no trials have been reported
Eradication of carriage	Ciprofloxacin	PO	—	500–750 mg bid	28 days	If eradication is indicated for public health reasons, a trial of medical therapy is justified, even in patients with evidence of cholelithiasis. Cholecystectomy may be considered.
	Amoxicillin	PO	75–100 mg/kg/day in 3 divided doses	2 g tid	4–6 weeks	Lower efficacy than fluoroquinolones but may be considered for treatment of carriage in individuals harboring strains with fluoroquinolone resistance.

[a]See text for references.
[b]Weight-based pediatric dosage should not exceed adult maximum.
[c]Recommended that treatment continue for at least 7 days after defervescence to minimize relapse.
NaR, Nalidixic acid resistant (see text); *TMP-SMX*, trimethoprim-sulfamethoxazole.
Modified from Magill AJ, et al., eds. *Hunter's Tropical Medicine and Emerging Infectious Diseases*. 9th ed. Philadelphia: Saunders; 2013:568–576.

Adjunctive Therapy

- high-dose dexamethasone: shock , significant mental status changes

Supportive Care and Management of Complications

- rehydration, nutritional management, mobilization
- Antipyretics: ibuprofen was superior to paracetamol
- intestinal hemorrhage: monitored (intensive care setting)
- Intestinal perforation: surgical intervention, Antibiotic regimens (intestinal microbiota, including anaerobes)

Chronic Carriage

- individuals whose occupation involves food handling

- ciprofloxacin: 28 d ,(80-90%)
- Cholecystectomy(cholelithiasis + resistant to prolonged antimicrobial therapy)
- Amoxicillin: high doses (75–100 mg/day for 4-6 weeks)

- trimethoprim-sulfamethoxazole with or without rifampin: ?

Prevention

- safe water/ adequate sanitation

- At a household level, hand washing with soap before preparing or eating food, avoidance of raw or uncooked foods, and local disinfection of unsafe drinking water, followed by storage in narrow-mouthed containers

- Vaccine

TABLE 102.5 Typhoid Fever Vaccines Currently Commercially Available Internationally

VACCINE	TYPE	ROUTE	DOSE AND INTERVAL	MINIMUM AGE	PROTECTION AGAINST *SALMONELLA* TYPHI	BOOSTING INTERVAL IN TRAVELERS
Ty21a	Live attenuated	Oral	Four doses (in United States) Administer one dose every other day until complete	6 years[a]	50%–80%[b]	Every 5 years
Vi capsule antigen	Polysaccharide	Intramuscular	1	2 years	50%–80%	Every 2 years
Vi tetanus toxoid conjugate vaccine	Polysaccharide conjugate	Intramuscular	1	6 months	80%–85%	Not yet defined
Vi CRM-197 conjugate vaccine	Polysaccharide conjugate	Intramuscular	1	6 months	Not yet defined	Not yet defined

[a]Per World Health Organization and US Advisory Committee on Immunization Practices.[194,195]

[b]Has some efficacy against *Salmonella* Paratyphi B (see text). Additional vaccines are under development, including conjugate vaccines.

Modified from Magill AJ, et al., eds. *Hunter's Tropical Medicine and Emerging Infectious Diseases*. 9th ed. Philadelphia: Saunders; 2013:568–576.

- آقای 35 ساله با تب از 5 روز قبل همراه با سردرد و یبوست مراجعه کرده است. مسافرت اخیر به میرجاوه داشته است. در معاینه تب 39 درجه داشته و به سوالات به خوبی جواب نمی دهد. در معاینه شکم اسپلنومگالی دارد.

توصیه شما چیست؟

- کشت خون وادرار
- CBC. SGOT. SGPT. LDH
- WIDAL
- سونوگرافی شکم و لگن

- چه درمانی توصیه می کنید؟
- بستری در بیمارستان
- آموکسی سیلین وریدی
- سیپروفلوکساسین خوراکی
- سفیکسیم خوراکی
- سفتریاکسون تزریقی

Non typhoidal salmonella(NTS)

Epidemiology

- Unlike *S.* Typhi and *S.* Paratyphi, can be acquired from multiple animal reservoirs
- *S.* Typhimurium and *S.* Enteritidis are the most common
- Incidence: highest during rainy season in tropical climates, warmer months in temperate climates
- Invasive NTS infection: <5 y, malaria, HIV, malnutrition, unclean drinking water sources

Transmission:

- consumption of food animal products (eggs, poultry, undercooked ground meat, dairy products, fresh produce contaminated with animal waste)
- contact with animals or their environment
- contaminated water.

Health care–associated salmonellosis

- Infrequent

Transmission:

- **foodborne**
- patients to **health care providers**: phlebotomy, handling soiled linen, noncompliance with barrier precautions, and fecally incontinent residents.
- health care providers to **patients**: low if infection control measures(hand hygiene, correct use of personal protective equipment, disinfection of patient-care equipment)
- **neonates** and infants from acutely or chronically infected family members
- Contaminated enteral feeding and crowding

Clinical manifestations

- Gastroenteritis
- enteric fever
- bacteremia and vascular infection
- localized infections
- chronic carrier state

outcomes, including case-fatality rates and hospitalization rates, differ substantially by serotype

Gasteroenteritis

- Self-limited, acute
- Incubation period: 6-48 h(7d)
- Most: loose, moderate volume, without blood
- watery and of large volume (“cholera-like”) or small volume associated with tenesmus (“dysentery-like”).
- Fever (38°–39°C), abdominal cramping, nausea, vomiting, chills , Headache, myalgias, and other systemic symptoms
- S/E: neutrophils , less frequently, red blood cells
- ➢ syndrome of pseudoappendicitis, inflammatory bowel disease, toxic megacolon
- Diarrhea resolves 3-7 d, fever 3d
- carriage in stool : 4- 5 w(adults), 7 w (children)
- Antimicrobial therapy may increase the duration of carriage

Bacteremia , vascular infections

Up to 8% of gastroenteritis develop bacteremia; of these, 5% to 10% develop localized infections

- serotypes Choleraesuis, Dublin, Enteritidis, Heidelberg, Poona, and Schwarzengrund
- Infant, elderly
- comorbidities, including immunosuppression

Endovascular infection

- **high-grade or persistent bacteremia**

- preexisting valvular heart disease, atherosclerotic vascular disease, prosthetic vascular grafts, or aortic aneurysms
- Mortality rates: 14-60%(lower with prompt diagnosis and combined medical and surgical therapy)
- fatal complications: valve perforation, endomyocardial abscess, infected mural thrombus, pericarditis, mycotic aneurysms, aneurysm rupture, aortoenteric fistula, and vertebral osteomyelitis.

Chronic Carrier State

- persistence of *Salmonella* in stool or urine for more than 12 months after acute infection.
- 0.2-0.6%
- associated with underlying host immunosuppression

Treatment : GE

- self-limited
- increased risk for invasive infection and may benefit from preemptive antimicrobial therapy

1- neonates (up to 3 m)
2- older than 50 y with suspected atherosclerosis
3- immunosuppression
4- cardiac valvular or endovascular abnormalities
5- significant joint disease

- oral or intravenous antimicrobial administered for 48-72 h or until the patient becomes afebrile
- Immunocompromised persons: 7 -14 d, fluoroquinolone
- oral therapy, fluoroquinolone, TMP-SMX, or amoxicillin

Bacteremia

- third-generation cephalosporin and a fluoroquinolone until susceptibilities are known

- High-grade bacteremia (>50% of three or more blood cultures testing positive): evaluation for endovascular abnormalities, with 6 weeks of IV ceftriaxone or IV ampicillin or by fluoroquinolone therapy (initially administered IV followed by oral when stable)
- Low-grade bacteremia: 7- 14 d, IV ceftriaxone or ampicillin (IV followed by oral, fluoroquinolone)
- Early surgical resection

TABLE 228.2 Extraintestinal Infectious Complications of Salmonellosis

SITE	INCIDENCE	RISK FACTORS	MANIFESTATIONS	COMPLICATIONS	MORTALITY	DIAGNOSIS	THERAPY
Endocarditis	0.2%–0.4%	Preexisting valvular heart disease	Valvular vegetation, infected mural thrombus	Valve perforation, relapse (20%–25%), pericarditis	~70%	Blood culture, echocardiography	Early valve surgery + 6 weeks P ceph 3, P ampicillin, or P, then PO fluoroquinolone
Arteritis	Rare	Atherosclerosis, aortic aneurysm, endocarditis, prosthetic graft, myelodysplasia	Prolonged fever, pain in back, chest, or abdomen	Mycotic aneurysm, aneurysm rupture, aortoenteric fistula, vertebral osteomyelitis	14%–60%	Blood culture, sonogram, MRI or CT	Early surgical intervention + 6 weeks P ceph 3, P ampicillin, or P, then PO fluoroquinolone
Central nervous system	0.1%–0.9%	Infants (especially neonates)	Meningitis, ventriculitis, brain abscess, subdural empyema, encephalopathy	Seizures, mental retardation, hydrocephalus, brain infarction, relapse	~20%–60%	CSF culture, CT or MRI	≥3 weeks P ceph 3, P ampicillin, or a carbapenem
Pulmonary	Rare	Lung malignancy, structural lung disease, sickle cell anemia	Pneumonia	Lung abscess, empyema, bronchopleural fistula	~25%–60%	Respiratory culture, chest radiograph	≥2 weeks P/PO abx
Bone	<1%	Sickle cell anemia, male gender, connective tissue disease, immunosuppression	Femur, tibia, humerus, lumbar vertebrae	Relapse, chronic osteomyelitis	Very low	Bone radiograph	≥4 weeks P ceph 3, P ampicillin, or P, then PO fluoroquinolone + surgery for sequestra
Joint, reactive	0.6%	HLA-B27, antimicrobial therapy	Joints (≥3) involved (especially knee, ankle, wrist, and sacroiliac)	Prolonged symptoms (mean duration, 5.5 mo)	Negligible	Joint fluid examination and culture	Nonsteroidal antiinflammatory agent
Joint, septic	0.1%–0.2%	Osteoarthritis, connective tissue disease, sickle cell disease, prosthetic joint	Knee, hip, shoulder	Joint destruction, osteomyelitis	Very low	Joint fluid examination and culture	Repeated needle aspiration + ≥4 weeks IV/PO abx
Muscle/soft tissue	Rare	Local trauma, male gender, diabetes, HIV infection	Abscess, pyomyositis	Osteomyelitis, endovascular infection, frequent relapse	~33%	Ultrasonography, aspiration	Drainage + ≥2 weeks P abx
Hepatobiliary	Rare	Cholelithiasis, cirrhosis, amebic abscess, echinococcal cyst, hepatocellular carcinoma	Hepatomegaly, cholecystitis, hepatic abscess	Rupture with secondary peritonitis, subphrenic abscess, spontaneous bacterial peritonitis	~10%	Ultrasonography, aspiration	Drainage + ≥2 weeks P abx
Splenic	Rare	Sickle cell anemia, splenic cyst, splenic hematoma	Splenomegaly	Left pleural empyema, subphrenic abscess, rupture with secondary peritonitis	<10%	Ultrasonography, aspiration	≥2 weeks P abx + percutaneous drainage or splenectomy
Urinary	0.6%	Urolithiasis, malignancy, renal transplant, elderly female	Cystitis, pyelonephritis	Renal abscess, interstitial nephritis, relapse	≈20%	Urine culture, ultrasonography	Removal of structural abnormality + 1–2 weeks P abx + ≥6 weeks PO fluoroquinolone or TMP-SMX
Genital	Rare	Pregnancy, renal transplant	Ovarian abscess, testicular abscess, prostatitis, epididymitis	Abscess	Very low	Ultrasonography, aspiration	Drainage of collection + 1–2 weeks P abx + ≥6 weeks PO fluoroquinolone or TMP-SMX
Soft tissue	<1%	Local trauma, immunosuppression	Pustular dermatitis, SC abscess, wound infection	Septic thrombophlebitis, endophthalmitis	~15%	Drainage culture	≥2 weeks P abx + drainage of collection

abx, Antibiotics; *CSF*, cerebrospinal fluid; *CT*, computed tomography; *HIV*, human immunodeficiency virus; *HLA*, human leukocyte antigen; *MRI*, magnetic resonance imaging; *P abx*, parenteral ampicillin; *P ceph 3*, parenteral third-generation cephalosporin; *PO*, oral; *P/PO abx*, parenteral or oral antibiotic (e.g., fluoroquinolone, ampicillin, TMP-SMX, or P ceph 3); *P/PO fluoroquinolone*, parenteral or oral fluoroquinolone; *SC*, subcutaneous; *TMP-SMX*, trimethoprim-sulfamethoxazole.

Control and prevention

- Vaccination of livestock and egg-laying hens
- limiting the use of antimicrobials as animal growth promoters
- improved food safety practices
- do not serve food containing raw or undercooked eggs, use pasteurized eggs
- avoid cross-contamination of food items
- good personal hygiene
- Maintenance of time-temperature standards for food handling

food handlers after gastroenteritis:

- Two consecutive negative stool samples(whose work involves touching unwrapped foods that are consumed raw or served without further cooking)

- Routine surveillance of food handlers for asymptomatic stool carriage of *Salmonella* is not recommended

health care–associated transmission:

- patients excreting NTS should be managed with standard precautions
  - hand hygiene
  - personal protective equipment(gloves, when performing direct patient care or handling fecally soiled articles)
  - enhanced environmental disinfection
  - cohorting of ill patients

- خانم 65 ساله با سابقه تعویض دریچه میترال و روماتیسم مفصلی با اسهال ابکی با حجم زیاد همراه با درد شکم وتهوع، از 3 روز قبل مراجعه کرده.
- در آزمایش مدفوع گلبول قرمز دیده نشده ولی گلبول سفید 8-10 عدد گزارش شده است.
- توصیه شما چیست؟

- دهیدراتاسیون
- درمان علامتی
- سیپروفلوکساسین 2-3 روز بعد از قطع تب