



A Review on Recent Trends in Diagnostic Test and Medication of Typhoid

1Unde Dushyant Vijay, 2Asst.Prof.Shubhangi Mali

1Student, 2Assistant Professor

1DBATU,

2DBATU

Abstract:

Typhoid fever is still a deadly disease in developing countries, mainly in India. Although, the paediatric population is mostly affected by this disease, yet the disease is an significant cause of morbidity and mortality in adult populations also. In India, most of the cases of typhoid fever are diagnosed clinically, or at the most by the Widal test which is not fool proof. The disease typhoid fever is an orally transmitted transferrable disease caused by the bacteria *Salmonella typhi*.

Following the growth period of 7 to 14 days, there is onset of fever and malaise. The fever is then attended by chills, headache, malaise, anorexia, nausea, vague abdominal discomfort, dry cough and myalgia. This review describes various diagnostic tests such as widal test, enzyme-linked immunosorbent assay(ELISA),Igm dipstick test, DNA detection,etc.And various treatments for typhoid fever are involved in this review like as antibiotics, vaccination,oral rehydration therapy,surgery,resistance,home care,treatment of carriers,antimicrobial therapy,supportive treatment,& medications pregnant women takes in typhoid.

Keywords: Typhoid Fever, Salmonella, Diagnosis, Widal test, Sensitivity, Treatment,etc.

Introduction:

Typhoid is an acute infective and risky disorder related with fever. It is caused by *Salmonella enteric* serovars Typhi, Paratyphi A, Paratyphi B, and Paratyphi C can also be cumulatively grouped as typhoidal *Salmonella*, whereas some are accumulate as non-typhoidal *Salmonella* [NTS]. Typhoid strains are people host-confined life forms that reason typhoid fever and paratyphoid fever together alluded to as enteric fever. In a few Asian countries, *Salmonella* strain Paratyphi A has represented a developing extent of enteric fever[1].200 years ago, one of the biggest cause of morbidity and death rates in the developed

world was typhoid fever or for that issue enteric fever. Due to advancements in sanitary and general health situation, the conditions have greatly improved now and the deadly disease of past years is very unusual and valuable now in the USA and the Europe [2].

➤ **Symptoms:**

The clinical presentation of typhoid fever varies from a mild illness with low fever, and slight dry cough to a severe clinical picture with abdominal uneasiness and multiple complications. Many factors control the severity and overall clinical effect of the infection. They include the duration of illness before the beginning of appropriate therapy, the choice of antimicrobial treatment, age, the previous contact or vaccination history, the virulence of the bacterial strain, the quantity of inoculums ingested, host factors (e.g. AIDS or other immunosuppressant) and whether the individual was taking other medications such as H2 blockers or antacids to reduce gastric acid. Patients who are infected with HIV are at considerably increased risk of clinical infection with *S. typhi* and *S. paratyphi*. Confirmation of *Helicobacter pylori* infection also represents an enhanced risk of acquiring typhoid fever [3].

Other symptoms

- Diarrhoea,
- Abdominal pain,
- Vomiting,
- Myalgia,
- Cough,
- Weight loss,
- Constipation,
- Abdominal warmth,
- Palpable spleen,
- Palpable liver
- Rose spots.

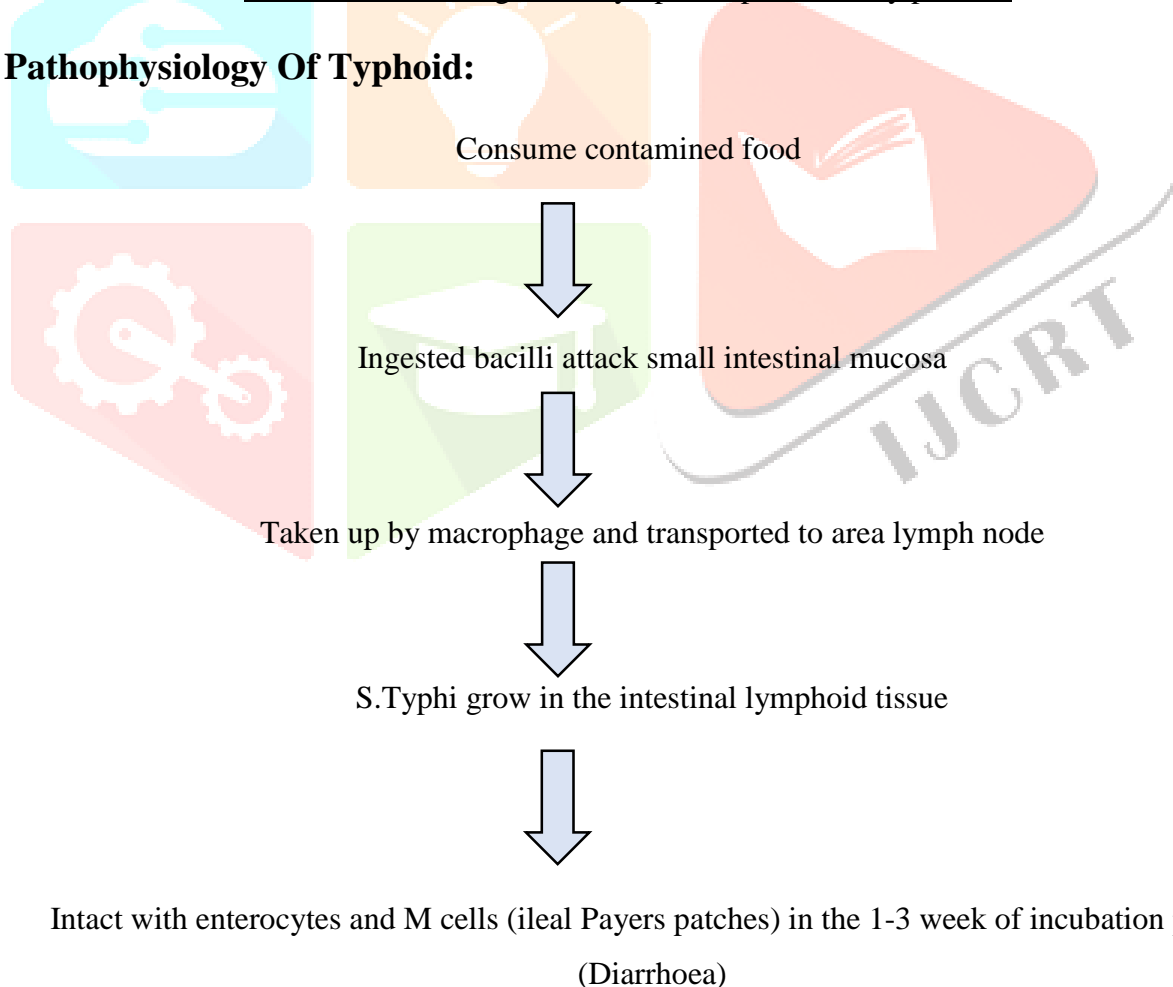


Reports were also made concerning *S. typhi* sepsis and rhabdomyolysis with acute renal failure and also on ileal damage in children. [4].

Sr.No.	Clinical Signs & Symptoms	Percentage of patients(numbers)
1.	Fever (>37.5 °C)	100 (200)
2.	Fatigue	38.5 (77)
3.	Headache	32.5(65)
4.	Anorexia	32.5(65)
5.	Joint pains	27 (54)
6.	Abdominal pain	23.5 (47)
7.	Vomiting	23 (46)
8.	Cough	19 (38)
9.	Diarrhoea	14.5 (29). [5]

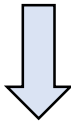
Table No. 1- Common clinical signs and symptoms presented by patients

➤ **Pathophysiology Of Typhoid:**

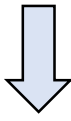


End of incubation period, bacilli penetrate blood stream (Bacteraemia phase)

(Onset of typhoid fever)



Bacteria infect the gallbladder, biliary system and lymphatic tissue of the bowel and multiply in high number



Then pass into the intestinal tract (stool)

➤ **Causes of Typhoid :**

- Typhoid is infected by a bacterium called Salmonella typhi.
- It is transmitted by: Contaminated food and water
- Typhoid carriers - some people still later than recovery hold the bacteria in their intestine or gallbladder
- The risk factors include: Close contact with contaminated person
- Drinking polluted water that contain Salmonella typhi.[6]

➤ **Other Countries Report of Typhoid Cases:**

In many countries like Europe and North America, the rate of typhoid fever is very less, while this disease is widely spread in developing countries, such as Africa, Latin America and South or Southeast Asia, the disease is endemic. Per annum, the cases of typhoid are around 5,700 in the United States and Indonesia; there are 573 cases per lakh people living in the country. Typhoid is bacterial infections that cause high fever, diarrhoea and vomiting. This disease is infected by Salmonella typhi or S. paratyphi (Whitaker, Franco-Paredes, Del Rio, & Edupuganti, 2009).

In developing countries, Enteric fever becomes a main public health issue now. Many of the cases occurred in Asia mostly in India where proper sanitation is very reduced and the cases of Typhoid are approximately 21 million and about 2,16,509 mortality cases appeared per year (Bassey & Izah, 2017). Salmonella Typhi and Paratyphi A cause the adverse infection. In many developing countries Enteric fever is common, In the Indian subcontinent, the death rate is increasing gradually if proper treatment not occurred. Including India and, if not treated properly, has a mortality rate of 30%. Effective medical care reduces the death rate as low as 0.5%. [7]

➤ **Contamination & Transmission**

Humans are the only usual host and reservoir. The infection is transmitted by intake of food or water contaminated with faeces. Ice cream is known as a significant risk factor for the spread of typhoid fever. Shellfish taken from infected water, and raw fruit and vegetables fertilized with dirt, have been sources of past outbreaks. The highest rate occurs where water supplies serve large populations are infected with faeces. Epidemiological data recommend that waterborne transmission of S. typhi

generally involves small inocula, whereas food borne transmission is related with large inocula and high attack rates over short periods.

The inoculum size and the type of vehicle in which the organisms are ingested greatly affect both the attack rate and the incubation period. In helpers who ingested 109 and 108 pathogenic *S. typhi* in 45 ml of skimmed milk, clinical illness appeared in 98% and 89% correspondingly. Doses of 105 caused typhoid fever in 28% to 55% of volunteers, while none of 14 persons who ingested 103 organisms developed clinical illness. Although it is widely believed that *Salmonella* is transmitted by means of the oral route, the transmission of *S. typhimurium* via the respiratory route has been established in a mouse model. [8]

➤ Infection of Salmonella to Various Organs:

The spread and movement of salmonellae to various organs. Gallbladder epithelial cells acts as a novel position for in vivo replication of *Salmonella* leading to the pathogenesis in the gallbladder during typhoid fever. *Salmonella* related to gall bladder cancer has been also invented by the researchers. Reports were also made about the hepatic involvement with typhoid and elevated serum bilirubin, and serum alanine transaminase level.

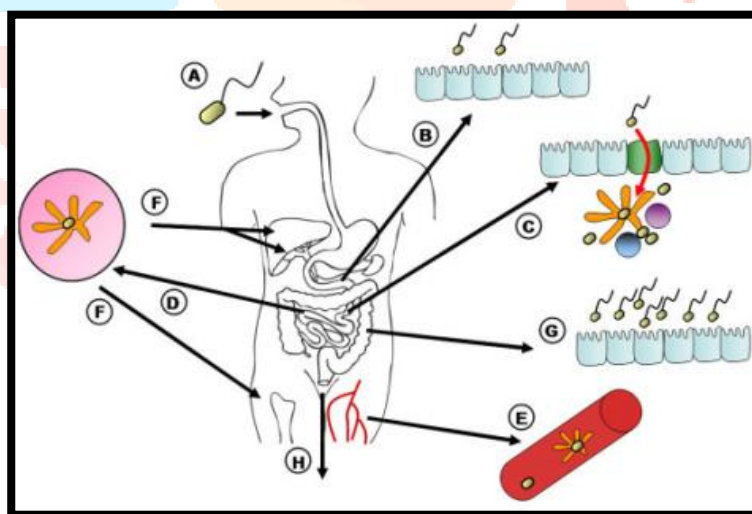


Fig No.1- Infection of Salmonella to various organs

Spleen is the secondary lymphoid organ of the body. It plays vital role in immune system. Spontaneous spleen rupture and splenic abscess have also been seen in this fever. This bacterium is also able to carry on in its host causing a chronic disease by colonizing the spleen and liver. The kidneys are organs and are store house of many functions. They belong to an important part of the urinary system. The kidney serves homeostatic functions such as the regulation of electrolytes, continuation of acid-base balance, and regulation of blood pressure. Renal association like bacteriuria, nephrotic syndrome and acute renal failure has been studied due to *S. paratyphi A*.

Salmonella infection is a active process in which the bacteria encounter many cell types and organs. Proper in vitro models are necessary for unravelling the pathogenic determinants functioning at different stages of the infection, and for developing new antimicrobials against Salmonella infections. Certain Salmonella serovars are restricted to human hosts or cause various diseases depends on whether infecting animals or humans. One such example is Salmonella Typhimurium, which causes gastroenteritis in humans, but typhoid-like disease in mice, making it complicated to understand data obtained from mouse experiments.

Salmonella infections induce intestinal inflammatory responses involving neutrophil in filtrations and the manufacture of pro-inflammatory cytokines. It has been shown that cytokine secretions were improved in monolayer and 3-D organotypic models of human colonic epithelium (HT-29) as well as in the C57BL/6 mouse model upon Salmonella infection. Further, more patients infected by Salmonella show gamma interferon (IFN- γ) induction together with superior tumor necrosis factor alpha (TNF- α). Using crypt-derived mouse enteroids, Zhang et al. were able to reproduce the Salmonella induced inflammatory responses. Further, more Salmonella infection induce the activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B) signalling pathway in the mouse enteroids accompanied by the expression of inflammatory cytokines including TNF- α and IFN- γ . This is in line with results from Salmonella infection, where genes encoding pro-inflammatory cytokines were tolerant.[4,9]

➤ **Diagnosis Of Typhoid:**

The diagnosis is generally established by identifying Salmonella typhi in a culture of your blood or other body fluid or tissue.

- **Body fluid or tissue culture**

For the culture, a small sample of your blood, stool, urine or bone marrow is kept on especial medium that encourages the growth of bacteria. The culture is check under a microscope for the presence of typhoid bacteria.

A bone marrow culture often is the most sensitive test for Salmonella typhi. While performing a culture test is the most common diagnostic test, other testing may be used to assumed typhoid fever infection, such as a test to invent antibodies to typhoid bacteria in your blood, or a test that checks for typhoid DNA in your blood.[10]

- **Stool Samples**

Stools can be collected from acute patients and they are particularly useful for the diagnosis of typhoid carriers. The isolation of S. typhi from stools is suggestive of typhoid fever. However, the clinical condition of the patient should be considered. Stool specimens should be collected in a sterile wide-mouthed plastic container. The probability of obtaining positive results increases with the quantity of stools collected. Specimens should first be processed within two hours after collection.

- **Serum**

For serological purposes, 1-3 ml of blood should be inoculated into a tube without anticoagulant. A second sample, if at all possible, should be collected at the convalescent stage, at least 5 days later. After clotting has occurred the serum should be separated and stored in aliquots of 200 ml at +4°C. Testing can take

place immediately or storage can maintain for a week without affecting the antibody titre. The serum should be frozen at -20°C if longer-term storage is essential. [11]

Serological Diagnosis of Typhoid Fever:

1. Widal test

The Widal test has got limitations such as the difficulty in analysis, the need to display a fourfold rise after a week and need of knowing the endemicity of the area. A fourfold rise in the Widal assay titre is therefore usually required for a definite serological diagnosis, and a second serum sample is infrequently obtained in regions where enteric fever is a major concern. It is indicative of typhoid fever in only 40-60% of patients at the time of admission. Test for the occurrence of Salmonella antibodies in the patients' serum may be of value in the diagnosis of enteric fever. The patients' serum is tested by agglutination method for its antibody titre against O, H and Vi suspensions of enteric fever bacteria, like *S. Typhi*, *S. paratyphi A* and *S. paratyphi B*. The test results are not easy to understand in areas where typhoid and other Salmonellosis are endemic.

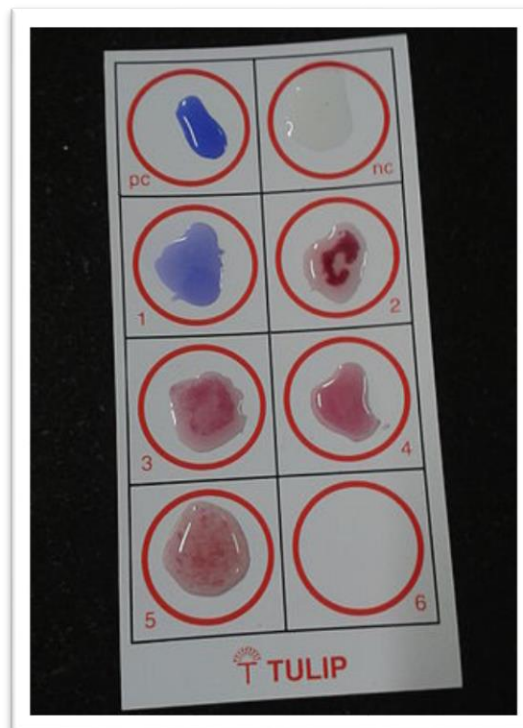


Fig No.2- Widal test Card

2. Enzyme-Linked Immunosorbent Assays (ELISA)

Enzyme-linked immunosorbent assays (ELISA) have been measured an alternative approach for the diagnosis of typhoid fever. The IgM response to effectively treated bacterial infections usually persists for only a few weeks or months. Demonstration of IgM antibodies to Salmonella antigen might therefore be of more diagnostic importance in an endemic population than detection of IgG. Though, there are theoretical limitations to the indirect ELISA for IgM. If the concentration of specific IgG in a sample is considerably greater than the concentration of IgM, it can produce false adverse results by competing for

the antigen determinants on the plate. Alternatively, an IgM-class rheumatoid factor that may be present in the sample can react with antigen-IgG complexes and produce a false-positive result.[12]

New diagnostic tests: current status and usefulness

▪ **IDL Tubex® test**

The Tubex® test is simple (effectively a one-step test) and quick (taking approximately two minutes). It exploits the simplicity and user-friendliness of the Widal and the slide latex agglutination tests but uses the separation of coloured particles in solution to progress resolution and sensitivity. Specificity is enhanced by means of an inhibition assay format and by detecting antibodies to a single antigen in *S. typhi* only. The O9 antigen used in the test is extremely specific because its immunodominant epitope is a very rare dideoxyhexose sugar that happens in nature. This antigen has been found in serogroup D salmonellae but not in other microorganisms.

▪ **DNA detection**

The detection of specific DNA sequences inside the genome of *S. Typhi* would appear to be an attractive proposition. Many *S. Typhi* PCR based assays have targeted the *fliC* gene, utilizing nested primers to enhance sensitivity [43-47]. There is an additional sensitivity benefit of PCR, in that it can hypothetically amplify DNA from dead or unculturable bacteria. Various PCR-based studies on typhoid suggest that the assay is specific and sensitive and relatively straight forward to perform. Indeed, such studies have yielded sensitivities >90%. Though, we believe PCR offers only limited potential for typhoid diagnostics. Now there is no validated PCR test in common use, only in-house systems which are open to at variance interpretation and none would meet the rigors of quality control to make this assay used worldwide. [13]

▪ **Typhidot**

On the other hand, the Typhidot depends on a subjective dab smudge catalyst connected immunosorbent measure that independently identifies the nearness of IgM and IgG in constant sera against a *Salmonella Typhi* particular 50 KD external film protein. Although the fact that Typhidot is quick, simple and reasonable, its utilization ought to be demoralized because of low affectability and specificity and immaterial connection to the illness [43] as found in the examination led in Pakistan in which they found that affectability of Typhidot was 26.7% and the specificity was 61.5% [14].

▪ **IgM dipstick test**

The typhoid IgM dipstick measure is proposed for the serological diagnosis of typhoid fever through identifying *S. Typhi* particular IgM antibodies in serum or whole blood tests. The measure comprises of a dipstick, a lyophilized non-enzymatic recognition reagent, fluid to reconstitute the identification reagent, fluid to wet the test segment of the dipstick before hatch with serum and location reagent, and test tubes. The segments are steady for a long time if put away in the temperature run 4-25°C of a dry place and shielded from guide presentation to sunlight. The examiner depends on the authoritative of *S. typhi*-particular IgM antibodies to *S. typhi* LPS antigen and the recoloring of bound antibodies by an against human IgM counter acting agent conjugated to colloidal color particles. The white test piece of the dipstick

contains the antigen immobilized in a particular line. The strip additionally has a control line with hostile to human IgM antibodies. [15]

General principles for the management of typhoid

- Rapid diagnosis and institution of suitable antibiotic treatment
- sufficient rest, hydration, and correction of fluid-electrolyte imbalance
- Antipyretic therapy as essential (such as paracetamol 120-750 mg taken orally every 4-6 hours)
- Adequate nutrition: a soft, easily digestible diet should be sustained unless the patient has abdominal distension or ileus
- Close attention to hand washing and limitation of close contact with susceptible individuals through acute phase of infection
- Regular follow-up and monitor for difficulties and clinical relapse (this may contain confirmation of stool clearance in non-endemic areas or in high risk groups such as food handlers) [16]

➤ Treatment Of Typhoid:

Important considerations for treatment are the prevention of severe problems and death, and prompt resolution of clinical disease. It is also significant to remove the organism promptly to avoid relapses and faecal carriage. More than 90% of patients are achieved at home with oral antimicrobials, bed rest, and close medical follow up. Patients with continuous vomiting, severe diarrhoea, or abdominal distension need admission to hospital and parenteral antibiotic therapy.

Typhoid fever should be a severe consideration in an endemic area when a fever lasts extended than a week, even by the fifth day if there is severe toxemia. The decision to send laboratory inquiries and initiate empirical antimicrobial therapy depends largely on clinical decision. First choice of antibiotic depends on the sensitivity patterns of *S typhi* and paratyphi isolates in the area. The isolates can be mostly classified as sensitive to first-line antimicrobials, multidrug resistant but nalidixic-acid sensitive, and nalidixic-acid resistant. [17]

1. Antibiotics

Bacterial infection can be lessened or removed by the use of antibiotics. Antibiotics are naturally occurring agents, which are produced by microorganisms and act on other bacteria. Synthetic antibiotics have been also been built to fight against microorganisms. A number of antibiotics so far used in salmonella's contamination have been identified. The antibiotic used has a number of side effects. Also the salmonellae often get resistant to it leading to multi drug resistant typhoid (MDRST).

Examples: 1. Ampicillin,

2. Chloramphenicol,

3. Co-trimoxazole

4. Ciprofloxacin

5. Azithromycin

Antibiotic	Route	Adult Dosage	Duration in Days
Chloramphenicol	Oral, IV	500 mg	14
Trimethoprim-Sulfamethoxazole	Oral, IV	160/800 mg	14
Ampicillin	Oral, IV,IM	50-100 mg in 4 doses	14

Table No. 2- Antibiotic Therapy for Typhoid

2. Vaccination

Treatment of typhoid fever is done by the use of antibiotics, but growing resistance rates to the primary agents used have been related with complications and increased severity of illness. The burden of typhoid fever remains high in poor settings, and increasing antibiotic resistance is making treatment costly. One plan for reducing the typhoid morbidity and mortality is vaccination. Therefore effective and cost-effective vaccination is the regulate measure required to fight this infectious disease. The vaccines used are not fully active. Some have low efficiency while other show high efficiency as concluded from literature survey. More over the vaccine so far created has got side effects.

Two typhoid disease vaccines are available in the United States.

- Oral vaccine: Can be given to persons at least 6 years old. It consists of four pills taken every other day and must be finished at least 1 week before travel.
- Injectable vaccine: Can be given to people at least 2 years old and must be given at least 2 weeks before travel.[18]

3. Oral Rehydration Therapy

The renewal of oral rehydration therapy in the 1960s provided a simple way to avoid many of the deaths of diarrheal diseases in general.

4. Surgery

It is usually showed if intestinal perforation occurs. One study found a 30-day death rate of 9% (8/88), and surgical site infections at 67% (59/88), with the disease problem borne predominantly by low-resource countries.[50] For surgical treatment, most surgeons choose simple closure of the perforation with drainage of the peritoneum. Small-bowel resection is shown for patients with multiple perforations. If antibiotic treatment fails to destroy the hepatobiliary carriage, the gallbladder should be resisted. Cholecystectomy is sometimes successful, particularly in patients with gallstones, but is not always successful in destroying the carrier state because of persisting hepatic infection.

5. Resistance

As resistance to Ampicillin, Chloramphenicol, Trimethoprim-Sulfamethoxazole, and streptomycin is now mutual, these agents are no longer used as first–line treatment of typhoid fever. Typhoid resistant to these agents is called as multidrug-resistant typhoid.

Ciprofloxacin resistance is an growing problem, especially in the Indian subcontinent and Southeast Asia. Many centres are ever-changing from ciprofloxacin to ceftriaxone as the first line for treating supposed typhoid originating in South America, India, Pakistan, Bangladesh, Thailand, or Vietnam. Also, it has been recommended that Azithromycin is better at treating resistant typhoid than both fluoroquinolone drugs and ceftriaxone. Azithromycin can be taken by mouth and is less exclusive than ceftriaxone, which is given by injection.

A distinct problem exists with laboratory testing for reduced susceptibility to ciprofloxacin; current recommendations are that isolates should be tested instantaneously against ciprofloxacin (CIP) and compared to nalidixic acid (NAL), that isolates sensitive to both CIP and NAL should be reported as "sensitive to ciprofloxacin", and that isolates sensitive to CIP but not to NAL should be reported as "reduced sensitivity to ciprofloxacin". But an analysis of 271 isolates found that around 18% of isolates with a decrease susceptibility to fluoroquinolone, the class which CIP belongs (MIC 0.125–1.0 mg/l), would not be detected by this method. [19]

6. Home care

Dehydration from diarrheais mutual with typhoid fever. So, you need to drink plenty of water and beverages with electrolytes. Your doctor may give you electrolyte packets to help with this. If your condition worsens and you have to go to the hospital, doctors may give you intravenous (IV) hydration.

7. Drugs Recommended by the Expert Panel for the Management of Enteric Fever

After going through treatment references by the World Health Organization (WHO), the Suggestion of Physicians of India (API), and the Indian Association of Paediatrics (IAP), the skilled advisory panel concluded that there was a need to simplify the choice of the drugs in the treatment of enteric fever. They totally declared that the fluoroquinolone (especially, ciprofloxacin and Ofloxacin) and cephalosporin's (specifically those of the third and fourth generation) are suggested for use as the first-line therapeutic agents. When factors such as intolerance to oral drugs, dehydration, extremes of age, and related comorbid conditions are present, parenteral treatment should be instituted. Once the condition of the patient stabilizes, she/he should gradually be decreased from parenteral therapy to oral drugs. With the defervescence period usually being about 5 days, any patient who is not replying adequately may be switched to a different drug after stopping the first, or the second drug may be added to the first one. However, at any point during the course of the sickness, patients may develop symptoms of developing problems, which should serve as red flags for the treating doctor.

8. Treatment of Carriers

A person is said to be a chronic carrier if s/he is asymptomatic, but his or her stool or rectal swab cultures test positive for the presence of *S. typhi*, a year after recovery.²² There are basically three types of carriers, namely convalescent carriers, who continue to shed bacilli in their faces for 3 weeks to 3 months; temporary carriers, who sheds bacilli for more than 3 months up to a year; and chronic carriers, who shed bacilli for more than a year.⁵⁶ The Vi (virulence) antibody test is of value when screening for carriers. The WHO recommends the use of ciprofloxacin 750 mg twice daily for 4 months or 52 weeks. It is not

recommended for use in pregnant women. It may be used in children only if the benefits outweigh the risks. [20]

9. Antimicrobial Therapy

The ideal antimicrobial drug for typhoid infection should be available for oral and intravenous use in adults and kids, cause defervescence and clinical improvement in 3–7 days, render blood and stool cultures negative during and after treatment, prevent relapses after treatment, and have a low occurrence of side effects and low cost. This treatment will both benefit the patients by curing them and prevent disease in near exposed persons by curtailing excretion of pathogens in stools. Prevention of death, which would occur in >10% of untreated patients, due to problems such as bleeding from intestinal ulcers, intestinal perforation, and shock, is an obvious goal of therapy.

Example – Fluoroquinolone [21]

Fluoroquinolones	Route	Adult dosage/ day	Duration in days
Ciprofloxacin	Oral/IV	500 mg	10-14
Norfloxacin	Oral	400 mg	10
Ofloxacin	Oral	400 mg	10
Pefloxacin	Oral,IV	400 mg	14

Table No.3- Antimicrobial Therapy by Fluoroquinolone

10. Avoiding infection

Even when the symptoms of typhoid have passed, it is still likely to be carrying the bacteria. This makes it tough to stamp out the disease, because carriers whose symptoms have finished may be less careful when washing food or interacting with others.

The following are some general rules trusted Source to follow in locations where typhoid is common to help minimize the possibility of typhoid infection:

- Drink bottled water, if possible carbonated.
- If there is no access to bottled water, boil available water for at least 1 minute before drinking.
- Be wary of eating anything that somebody else has handled.
- Avoid eating at road food stands, and only eat food that is still hot.
- Do not have ice in drinks.
- Avoid uncooked fruit and vegetables, peel fruit yourself, and do not eat the peel.[22]

11. Treatment of Recurrent Typhoid Infection in Persons with Acquired Immunodeficiency**Syndrome**

In persons with AIDS and a first episode of *Salmonella* bacteraemia, 1 to 2 weeks of intravenous antimicrobial therapy followed by 4 weeks of oral quinolone therapy (e.g. ciprofloxacin, 500 to 750 mg twice daily) should be administered in an attempt to eradicate the organism and decrease the risk of recurrent bacteraemia. Persons who relapse after 6 weeks of antimicrobial therapy should receive long-term suppressive therapy with a quinolone or trimethoprim-sulfamethoxazole. Quinolone and zidovudine have a synergistic antibacterial effect against *Salmonella*; administration of both drugs may dramatically decrease the risk of recurrent infection. Although data are lacking, because of its efficacy in the prevention of *Pneumocystis carinii* infection, trimethoprim-sulfamethoxazole may be a good choice for long-term suppressive therapy for Salmonellosis if the organism is susceptible. [23]

12. Management of complications

Both outpatients and inpatients with typhoid fever should be closely monitored for the development of complications. Timely interference can prevent or reduce morbidity and mortality. The parenteral fluoroquinolone are probably the antibiotics of choice for severe infections but there have been no randomized antibiotic trials. In severe typhoid the fluoroquinolone are given for a minimum of 10 days. Typhoid fever patients with changes in mental status, categorized by delirium, obtundation and stupor, should be immediately evaluated for meningitis by examination of the cerebrospinal fluid. If the findings are normal and typhoid meningitis is suspected, adults and kids should immediately be treated with high-dose intravenous dexamethasone in addition to antimicrobials. If dexamethasone is given in an early dose of 3 mg/kg by slow i.v. infusion over 30 minutes and if, after six hours, 1 mg/kg is administered and subsequently repeated at six-hourly intervals on seven further occasions, mortality can be reduced by some 8090% in these high-risk patients. Hydrocortisone in a lower dose is not effective. High-dose steroid treatment can be given before the results of typhoid blood cultures are available if other causes of severe disease are unlikely. [24]

13. Medications Pregnant Woman Take in Typhoid

- Drug Combinations.
- Chloramphenicol.
- Ampicillin.
- Trimethoprim, Sulfamethoxazole Drug Combination.
- Trimethoprim. Sulfamethoxazole.

Risk Factors for Typhoid Fever during Pregnancy-

I. Decreased gastrointestinal motility
▪ Delayed gastric emptying
▪ Oesophageal reflux resulting in the use of acid-reducing or neutralizing medication
▪ Dilation of gallbladder

▪ Increase in biliary sludge
▪ Constipation
II. Increased production of red blood cell mass
Increased bone marrow activity and blood supply
III. Modulation of cell-mediated immunity
IV. Alterations in olfactory and gustatory sense
▪ Changes in appetite and food selection: pica
▪ Nausea and vomiting of pregnancy. [25]

Table No. 4- Risk Factors for Typhoid during Pregnancy

14. Supportive Treatment

- Antipyretics as required
- Adequate rest, hydration, and improvement of fluid-electrolyte imbalance
- Adequate nutrition: a soft, simply digestible diet should be continued unless the patient has abdominal distension or ileus
- In case of severe disease monitor blood pressure, blood sugar, electrolytes, hemoglobin , platelet counts and liver functions as indicated.[26]

➤ Prevention of Typhoid:

1. Safe Water-

Typhoid fever is a waterborne disease and the main preventive measure is to confirm access to safe water. The water needs to be of super quality and must be sufficient to supply all the community with sufficient drinking water as well as for all other domestic purposes such as cooking and washing.

2. Food Safety-

- Washing hands with soap before preparing or eating food
- Avoiding raw food, shellfish, ice
- Eating only cooked and still hot food or re-heating it

3. Sanitation-

- Appropriate facilities for human waste disposal must be available for all the community. In an emergency, pit latrines can be quickly built.
- Collection and treatment of sewage, especially during the rainy season, must be implemented
- In areas where typhoid fever is known to be present, the use of human excreta as fertilisers must be dejected.

4. Health Education-

In health facilities, all staff must be repeatedly educated about the need for:

- Excellent personal hygiene at work
- Isolation measures for the patient
- Disinfection measure.[27]

Future Aspects of Typhoid Medication:

- A new VI conjugate vaccine bound to nontoxic recombinant *Pseudomonas aeruginosa* has enhanced immunogenicity in adult and children aged 5-14 years. It is recently evaluated in Vietnam and the efficacy of vaccine in children aged 2-5 years after 27 month found 91.2 percent. 2, 3 an important advantage of this vaccine is that it has the potential to be immunogenic in infants under the age of two. 2 Currently DNA vaccine of typhoid fever is in phase 1 and 2 clinical trial. It shows 88% efficacy.
- The Permanent treatment of typhoid is antibiotics. Doctors most commonly use ciprofloxacin (Cipro) for non-pregnant women. Other antibiotics a physician may use are: Chloramphenicol (Chloromycetin). The use of these antibiotics may increase in future.

Conclusion:

Even today, enteric fever is a global public health problem, mainly in developing countries. Studies show the number of urban cases of typhoid is around 800-900/year. Widal test, though cheap and available should be understood with caution. We should be aware about the higher occurrence of typhoid fever in India and other developing countries. Huge movements should be initiated to make people understand the preventive measures, role of vaccines, importance of visiting doctors and the like.

Doctors should be conscious about the progressively developing antibiotic resistance and the emerging safe and effective newer antibacterial agents. The latter includes newer Fluoroquinolone and Macrolides in large doses, and finally third generation cephalosporin's both in oral and Injectable forms. Over and above, the profession should look forward to newer curative and preventive measures.

Reference:

1. Nusrat Yasin, Azmat Jabeen, Iqbal Nisa, Umber Tasleem, Hasan Khan, Faiza Momin, Faisal Shah, Ubaid Rashid, Umar Zeb, Aziz-ur-Rehman Safi, Mubashir Hussain, Muhammad Qasin, Hazir Rahman. A Review: Typhoid Fever, Journal of Bacteriology Infectious Diseases, March 2018; Volume.2; Issue.2, Page No. 1-7.
2. Uttam Kumar Paul, Arup Bandyopadhyay, Typhoid Fever: A Review, International Journal of Advances in Medicine, Volume.4; Issue.2 March-April 2017; Page No. 300-306.
3. Dr Camilo Acosta, Dr M. John Albert, Background document: The diagnosis, treatment and prevention of typhoid fever, World Health Organization, Page No. 1-38.
4. Kishwar Hayat Khan, Recent trends in typhoid research- A Review, International Journal of Biosciences (IJB), Vol. 2, No. 3, Page No. 110-120.
5. Emmanuel Fru Nsutebu, Peter Martins and Dieudonne Adiogo, Short communication: Prevalence of typhoid fever in febrile patients with symptoms clinically compatible with typhoid fever in Cameroon, Journal Of Tropical Medicine and International Health, volume 8 no 6, june 2003, Page No. 575-578.
6. [causes of typhoid - Search \(bing.com\)](#)
7. Syed Rizwan Abbas, Qurat ul Ain, A review paper on medicinal plants for Typhoid, Journal of natural sciences, Vol.8 : Issue 2, Page NO. 98-103.
8. Ivanoff B, Cordel J, Robert D, Fontanges R. Importance de la voie respiratoire dans la salmonellose expérimentale de la souris Balb/c. Comptes Rendus de l'Académie des Sciences (Paris) 1980: 1271-4
9. Yuebang Yin, Daoguo Zhou, Organoid and Enteroid Modeling of *Salmonella* Infection, Journal Of Frontiers in Cellular and Infection Microbiology, April 2018 | Volume 8 | Article 102, Page No. 1-13.
10. [Typhoid fever - Diagnosis and treatment - Mayo Clinic](#)
11. Dr Asma Ismail, Dr Keith Klugman, The diagnosis, treatment and prevention of typhoid fever, World Health Organization, Page No.8.
12. AFM Arshedi SATTAR1 , M Abdullah YUSUF2 , M Bodrul ISLAM3 , Waseka Akhter JAHAN4, Different Diagnostic Procedure of Typhoid Fever: A Review Update, Journal of Current and Advance Medical Research, July 2014 ; vol.1, issue 2, Page No. 35-41.

13. Stephen Baker^{1,2*}, Michael Favorov³, Gordon Dougan, Searching for the elusive typhoid diagnostic, BMC Infectious Diseases;2010, Page No. 2-8.
14. Morinigo MA, Muñoz MA, Martinez Manzanares E, et al. Laboratory study of several enrichment broths for the detection of Salmonella spp. particularly in relation to water samples. J Appl Bacteriol 1993;74:330-335.
15. Song JH, Cho H, Park MY, et al. Detection of Salmonella typhi in the blood of patients with typhoid fever by polymerase chain reaction. JCM 1993; 31:1439-1443.
16. [Current concepts in the diagnosis and treatment of typhoid fever - PMC \(nih.gov\)](#)
17. M K Bhan, Rajiv Bahl, Shinjini Bhatnagar, Typhoid and paratyphoid fever, Journal of THE LANCET, Vol 366 August 27, 2005, Page NO. 749-762.
18. Kashmiri A. Datea,*, Adwoa Bentsi-Enchill b, Florian Marks c, Kimberley Fox, Typhoid fever vaccination strategies, Elsevier:2015, Page No. 1-7.
19. [Typhoid fever - Wikipedia](#)
20. Rajesh Upadhyay, Milind Y Nadkar, A Muruganathan, Mangesh Tiwaskar, Deepak Amarapurkar, NH Banka, Ketan K Mehta, BS Sathyaprakash, API Recommendations for the Management of Typhoid Fever, Journal of The Association of Physicians of India, Vol.63, November 2015.
21. T. Butler, Treatment of typhoid fever in the 21st century: promises and shortcomings, Clinical Microbiology and Infection; July 2011, Vol. 17, Issue 7, Page No. 959-963.
22. <https://www.medicalnewstoday.com/articles/156859>
23. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4923770/>
24. <https://www.glowm.com/pdf/WHOdiagnosis%20treatment%20prevention%20of%20typhoid%20fever-2003-CustomLicense>
25. Faraj Touchan, John D Hall, and Richard V Lee, Typhoid fever during pregnancy: case report and review, Obstetric Medicine, The Royal Society of medicine Journal, Dec.2009, Vol.2, Issue 4, Page No. 161-163.
26. Prof. Bushra Jamil, Dr Summiya Nizamuddin, Typhoid Management Guidelines, Medical Microbiology and Infectious Diseases Society of Pakistan, 2021-22.
27. Dr Asma Ismail, Dr Keith Klugman, The diagnosis, treatment and prevention of typhoid fever, World Health Organization,2003,Page No. 1-38.