

Diagnosis Infection of *Salmonella Typhi*

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Introduction

Gram-negative bacteria that answerable for typhoid fever, enteric fever, is *Salmonella enterica* serotype typhi and has been a burden on developing countries for generations. In 1829, the first to invent the term “typhoid fever” after identifying lesions in the abdominal lymph nodes of patients who had died from “gastric fever.” by Pierre Louis [1]. 27 million typhoid fever infection and 217,000 death cases estimated yearly caused by *S. typhi* [2]. Infection cycle with *S. typhi* occur by the fecal-oral method; after eating, bacteria cross the intestinal epithelium able of colonizing the gallbladder, enter the bloodstream, and systemically multiply leading to chronic asymptomatic shedding [3]. Virulence factor of a gram-negative bacterial is outer membrane lipopolysaccharide (LPS), LPS is consist of lipid A tail; a core carbohydrate; and the bacterial cell protects from the innate immune system actions that occur caused by O-antigen side chain [4]. In 1896 diagnostic test developed commonly utilized for typhoid fever, enteric fever and measures agglutinating antibodies in the patient serum against the LPS and flagella H antigens of *S. typhi* is widal test; the test was still broadly used [5]. Other fast available serologic tests are Tubex and Typhidot assays. In principle, detects IgM antibodies response to O9 antigen *Salmonella* infection by Tubex test, but Typhidot test detects both IgM and IgG antibodies to *S. typhi* antigen, should be functional in identifying early acute illness [6].

Salmonella typhi

Salmonella enterica serotype typhi is a gram-negative belongs to the family *Enterobacteriaceae*, facultative anaerobe, rod-shaped, motile, flagellated bacterium whose only reservoir is the human body (Figure1)[7]. *Salmonella* is strictly non lactose fermenting when growth on MacConkey and no gas produces when grown in TSI media additionally Eosin-methylene blue (EMB) agars used for bacteria diagnostic identification, which are used to separate it from different *Enterobacteriaceae*.



Figure1: *Salmonella typhi*

Habitats

The intestinal tract of humans and animals is the central habitat of the *Salmonella*. Human or animal excretion are disseminated of *Salmonella* in the natural environment [soil, water, sometimes plants utilized as food]. They can excrete *Salmonella* either when clinically ailing or after having had salmonellosis, if they stay carriers. *Salmonella* organisms might survive a few years in soil and a number of weeks in water if conditions of pH, temperature, furthermore moisture are approving. Anyhow they don't appear to multiply essentially in the out of digestive tracts [8].

Virulence factor

Salmonella typhi is an efficient pathogen because it has a union of characteristics. This species contains Vi antigen, also an endotoxin will be expansion virulence. As well as invasins protein excretes that non permits phagocytosis cells to capture up bacteria. It is too ready to making innate immune response ineffective by that oxidative restraint of leukocytes.

Pathology

The infection of typhoid or, enteric fever caused by infection of *Salmonella typhi*. This illness is described by symptoms[9], usually initiate 6 to 30 days after exposure, also may contrast from quiet to harsh[10] [11], include: elevated fever over several days, abdominal pain, headaches, loss of appetite, nausea, mild vomiting, constipation or diarrhea is uncommon. Some people expand rose colored spots with a skin rash. Meningitis or general discomfort symptoms may be appeared last weeks or months when devoid of treatment. Other people don't appear affected although might be a bear the bacterium; however, they are still capable to reach the disease to others[12].

Antigenic structure[13]

The genus *Salmonella* is serologically positive for somatic lipopolysaccharide (O antigen), O antigens are resistant to alcohol also constant of heat, and also polysaccharide capsular (Vi antigen), as well as flagellar (H antigen) are heat-labile proteins (Figure2).

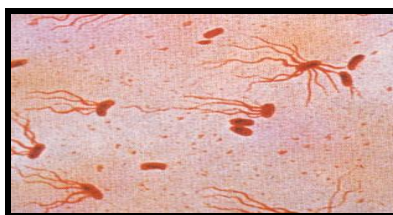


Figure2: O , Vi and H antigens of *S. typhi*

Diagnosis

Typhoid or paratyphoid fever disease results in a awfully low-quality septicemia, therefore diagnosis usually is accomplished by blood culture positive in only half the cases. The diagnostic bone marrow culture increases to about 80% of cases. During the acute phase of the infection the diagnosis stool cultures usually is appeared not positive. Therefore, the diagnosis of people with

acute infection typhoid used the traditional widal test (discover agglutinating specific IgM and IgG antibodies in serum patient against O and H antigens of *Salmonella*) [14] [15].

- **Widal test**

The serum in this test of patient is mixed with specific antigens dead *Salmonella* suspension. The positivity of the test when shown agglutinating which the serum patient is found specific antibodies against those antigens of *Salmonella*. If agglutinating doesn't happen in that case the negative test. The widal test is unreliable, prone to false positive results, time-prolonged, and in the early course of disease the test may be falsely negative. But due to its low cost broadly utilized in developing countries[16]. Newer fast serologic chief commercial assays are rather extra susceptible and specific, but are rarely existing, include the Tubex and Typhidot assays than the Widal test.

- **Tubex assays**

The Tubex test is a rapid immunochromatographic test that detects immunoglobulin M [IgM] antibodies to the O:9 antigen [the major antigenic determinant of *S. typhi* LPS]. Tubex test consist of two sorts of particles blue indicator particles covered with O9 antibody and brown magnetic particles covered with antigen. The positivity test is demonstrates whether serum patient contain antibodies connected to the brown magnetic particles and stay down at the bottom and the blue marker particles stay up in the solution giving a blue color. But the negative test is mean don't have typhoid when the serum doesn't have an antibody then the blue particle gets connected of the brown particles and giving no color and stay down at the bottom to the solution[17]. An advantage of this approach is that T-cell-independent IgM responses that target *S. enterica* O polysaccharide develop early in the clinical disease.

- **Typhidot assay**

The Typhidot test that detects both specific IgM and IgG antibodies to a specific 50-kDa *S. typhi* antigen [18]. The kit consists pad contain colloidal antigens(anti-human IgM or anti-human IgG). When the serum patient contains IgG and IgM antibodies specific antigen of *S. Typhi* and react with those antigens pad get turned into red color. This complex are here giving a pink-purplish colored band caused by go on to progress forward and the IgG and IgM antibodies will get attached to the first test line where IgG and IgM antigens. The control line consists of rabbit anti-mouse antibody when the complex will go on to progress more and reach the control line to indicate reagent color and a proper migration. After 2–3 days from disease when diagnosis by typhidot test that appeared two colored bands indicate a positive test. Negative test when appeared single-band of control line. Not bands at all indicates unacceptable tests. The result test is only negative or positive that it is not quantitative (Figure3)[19].

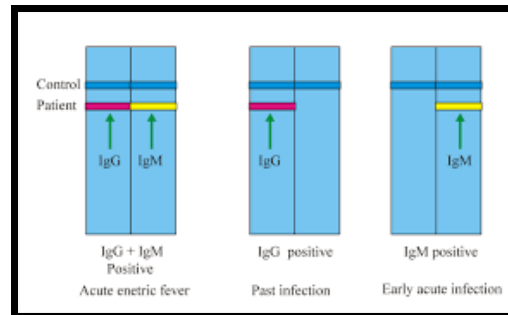


Figure3: Typhidot assay

References

1. Barnett R. Typhoid fever. *Lancet*. (2016) Nov 19;388[10059]:2467.
2. Crump JA, Luby SP, Mintz ED. (2004). The global burden of typhoid fever. *Bull World Health Organ* 82:346–353.
3. Snyder MJ, Hornick RB, McCrumb FR, Jr, Morse LJ, Woodward TE. (1963). Asymptomatic typhoidal bacteremia in volunteers. *Antimicrob Agents Chemother [Bethesda]* 161:604–607.
4. Murray GL, Attridge SR, Morona R. (2006). Altering the length of the lipopolysaccharide O antigen has an impact on the interaction of *Salmonella enterica* serovar Typhimurium with macrophages and complement. *J Bacteriol* 188:2735–2739.
5. Holzer SU, Schlumberger MC, Jackel D, Hensel M. (2009). Effect of the O-antigen length of lipopolysaccharide on the functions of Type III secretion systems in *Salmonella enterica*. *Infect. Immun.* 77:5458–5470.
6. Nicholas A. Feasey, Melita A. (2014). Gordon, in *Manson's Tropical Infectious Diseases [Twenty-third Edition]*
7. Crump JA, Sjölund-Karlsson M, Gordon MA, Parry CM. (2015). Epidemiology, Clinical Presentation, Laboratory Diagnosis, Antimicrobial Resistance, and Antimicrobial Management of Invasive *Salmonella* Infections. *Clin. Microbiol. Rev.* Oct;28[4]:901-37.
8. Parry CM, Hien TT, Dougan G, White NJ, Farrar JJ. (2002). Typhoid fever. *N. Engl. J. Med.* Nov 28;347[22]:1770-82.
9. Wain J, Hendriksen RS, Mikoleit ML, Keddy KH, Ochiai RL (March 2015). "Typhoid fever". *Lancet*. **385** (9973): 1136–45.
10. Anna E. Newton (2014). *"3 Infectious Diseases Related To Travel"*. CDC health information for international travel 2014: the yellow book. ISBN 9780199948499. Archived from the original on 2015-07-02.
11. "Typhoid Fever". cdc.gov. May 14, (2013). Archived from the original on 6 June (2016). Retrieved 28 March (2015).
12. "Typhoid vaccines: WHO position paper" (PDF). (2008). *Releve Epidemiologique*

Hebdomadaire. 83 (6): 49–59. February

- 13- Kenneth Todar, *Salmonella* and Salmonellosis
14. House D, Wain J, Ho VA, Diep TS, Chinh NT, Bay PV, Vinh H, Duc M, Parry CM, Dougan G, White NJ, Hien TT, Farrar JJ. (2001). Serology of typhoid fever in an area of endemicity and its relevance to diagnosis. *J Clin Microbiol* 39:1002–1007.
15. Rebecca W. Acosta, ... Victor Balaban, .(2009). In CDC Health Information for International Travel .
16. "Widal Test - an overview | ScienceDirect Topics". *www.sciencedirect.com*. Retrieved (2019)-11-14.
- 17 - "TYPHIDOT Rapid IgG/IgM (Combo)" (PDF). (2019). *Reszon Diagnostics International*. Retrieved 14 November.
18. Jason B. Harris, Edward T. Ryan,. (2015). In Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases [Eighth Edition].
19. Lim, Pak-Leong; Tam, Frankie C. H.; Cheong, Yuet-Meng; Jegathesan, M. (August 1998). "One-Step 2-Minute Test To Detect Typhoid-Specific Antibodies Based on Particle Separation in Tubes". *Journal of Clinical Microbiology*. **36** (8): 2271–2278.