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Interaction between Pathogenic Mechanism of *Salmonella* and Host Immune System

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Abstract *Salmonella* is a bacterium that widely exists in the natural world and can cause various diseases such as gastroenteritis and septicemia. *Salmonella* invades host cells through its virulence factors, such as serine, endotoxins, and flagella, disrupting the signaling pathways of host cells and evading surveillance and attack by the host immune system. *Salmonella* can also produce various molecules, such as surface proteins and lipopolysaccharides, to activate the host immune system's inflammatory response, leading to the formation of inflammatory lesions. Furthermore, *Salmonella* infection can affect both cellular and humoral immunity of the host immune system. Studies have found that *Salmonella* infection can result in reduced functionality of macrophages and dendritic cells, inhibition of T cell activation and proliferation, thereby weakening the host immune system's resistance. The research also introduces the diagnosis and treatment methods for *Salmonella* infection, including bacterial culture, molecular biology detection, and antibiotic therapy, and provides prospects for the study of the pathogenic molecular mechanisms of *Salmonella* and the interaction with the host immune system. Future research needs to further explore the virulence factors and immune evasion mechanisms of Salmonella, investigate the strategies of the host immune system's response, and provide a more scientific basis for the prevention and treatment of *Salmonella* infection.
Keywords *Salmonella*; Pathogenic mechanism; Immune escape; Host immune system; Prevention and treatment

Salmonella is a gram-negative bacterium widely distributed in nature, mainly existing in the intestines and environment of animals. It can cause human infection through eating contaminated food or drinking water, contact with infected animals or their feces, etc. The symptoms of *Salmonella* infection include diarrhea, fever, abdominal pain, nausea, vomiting, etc. In severe cases, it may also cause serious complications such as sepsis, organ damage, and pneumonia. Globally, millions of people are infected with *Salmonella* every year, and tens of thousands of people die, seriously affecting human health and life safety (Avondt et al., 2015).

The molecular mechanism of *Salmonella* infection and the interaction with the host immune system is one of the hot topics in recent years. The virulence factors of *Salmonella* mainly include serotonin, endotoxin, flagella, etc. Among them, serotonin is a molecule that can cause intestinal inflammation, which can promote *Salmonella* invasion into host cells and inhibit the inflammatory response of the host immune system. Endotoxin is a molecule that causes inflammatory responses, which can activate the inflammatory response of the host immune system, but also cause damage to host tissues. Flagella is a locomotive organ of *Salmonella* that can help *Salmonella* evade the attack of the host immune system. In addition, *Salmonella* can produce various molecules, such as surface proteins, lipopolysaccharides, etc., to activate the inflammatory response of the host immune system and form inflammatory foci. At the same time, *Salmonella* infection can also cause immune evasion of the host immune system. *Salmonella* can evade the surveillance and attack of the host immune system by interfering with the signal transduction pathway of host cells. In addition, *Salmonella* infection can also affect the cellular and humoral immunity of the host immune system. It has been found that after *Salmonella* infection, the functions of macrophages and dendritic cells in the host immune system are inhibited, and the activation and proliferation of T cells are also inhibited, thus reducing the resistance of the host immune system (Jantsch et al., 2011).

In terms of the diagnosis and treatment of *Salmonella* infection, there are currently multiple methods and means available. For example, bacterial culture, molecular biology detection, and antibiotic treatment. Among them, bacterial culture is currently the most commonly used method, but it has a higher time and cost, and there is a certain rate of misdiagnosis. Molecular biology detection can rapidly and accurately detect the presence of Salmonella, but it requires more professional experimental conditions and equipment. Antibiotic treatment is one of the conventional methods for *Salmonella* infection, but due to the abuse and improper use of antibiotics, there have been multiple drug-resistant *Salmonella* strains, which bring certain challenges and difficulties to treatment. Therefore, in-depth research on the molecular mechanism of *Salmonella* pathogenesis and the interaction with the host immune system, exploring the pathophysiological process and treatment methods of *Salmonella* infection, is one of the important directions of medical research today. I believe that with continuous exploration and efforts, there will be more breakthroughs in the future, providing more scientific and effective methods and means for the prevention and treatment of *Salmonella* infection.

1 Basic Characteristics of *Salmonella*

1.1 The traditional liquor brewing process and its characteristics

Salmonella is a gram-negative bacterium and a common enteropathogen. Based on the analysis of 16S rRNA sequences, *Salmonella* can be divided into two subgenera: *Salmonella* subgenus and Citrobacter subgenus (Denise et al., 2004). Among them, the *Salmonella* subgenus includes common *Salmonella* strains, with more than 2 500 different serotypes. They share common pathogenicity and can cause different symptoms ranging from mild diarrhea to severe sepsis. The Citrobacter subgenus includes some enteric bacteria related to Salmonella, such as Paratyphi and Lactobacillus acidophilus (Denise et al., 2004).

The morphological structure of *Salmonella* is similar to that of other gram-negative bacteria, with cells that are short rods with a size of approximately 0.7~1.5 micrometers × 2~5 micrometers. It has various virulence factors such as collagenase and lipopolysaccharide. *Salmonella* has flagella and a capsule on its surface, and the flagella can help it locate on the intestinal mucosa and invade host cells. The capsule can help *Salmonella* defend against the attack of the host immune system and enhance its pathogenicity. *Salmonella* colonies are grayish white or light yellow, with a smooth surface and neat edges, and sometimes secrete mucus (Figure 1). *Salmonella* is widely distributed in nature, mainly found in the intestines of animals and the environment, such as water, soil, plants, and food (Denise et al., 2004). *Salmonella* can cause human infections through eating contaminated food or drinking water, or contact with infected animals or their feces. The high-risk population for *Salmonella* infection includes young children, the elderly, and immunocompromised individuals. Globally, millions of people are infected with *Salmonella* each year, and tens of thousands die, seriously affecting human health and life safety. Therefore, preventing and controlling *Salmonella* infections is of great significance.

1.2 The growth characteristics and metabolic pathways of *Salmonella*

The growth characteristics and metabolic pathways of *Salmonella* have many similarities with other bacteria. *Salmonella* is an obligate anaerobe that can grow under low oxygen or anaerobic conditions. It can grow on various culture media, such as ordinary nutrient agar culture media and Escherichia coli selective agar culture media. Under suitable temperature and pH conditions, *Salmonella* can multiply rapidly and form colonies.

Salmonella has a relatively diverse metabolic pathway and can utilize various organic and inorganic substances as carbon sources, nitrogen sources, and energy sources. *Salmonella* can metabolize various monosaccharides and disaccharides, such as glucose, fructose, lactose, and sucrose. It can also utilize complex organic substances such as fatty acids, amino acids, and peptides for metabolism. Additionally, *Salmonella* can utilize inorganic substances such as sulfates and nitrites for metabolism. In the metabolic pathway, the oxidative phosphorylation pathway is the main energy source for *Salmonella*. In this pathway, *Salmonella* oxidizes substrates to CO2 and H2O, releasing energy through enzymes such as ATP synthase. At the same time, *Salmonella* can also perform anaerobic respiration to obtain energy by oxidizing inorganic substances such as sulfates and nitrites (Behnsen et al., 2015).

Figure 1 *Salmonella* electron microscopic image (*Salmonella* Testing Technique, 2021)

The growth characteristics and metabolic pathways of *Salmonella* have strong adaptability and diversity. It can utilize various organic and inorganic substances for metabolism, adapting to different environmental conditions and nutritional sources. This also provides a certain basis for *Salmonella* to survive and spread in the intestines or environment.

1.3 The virulence factors of *Salmonella* and their mechanism of action

As a Gram-negative bacterium, *Salmonella* is one of the commensal bacteria in the intestines of humans and animals. Although *Salmonella* is not harmful to the human body under normal conditions, when they enter and multiply in the human body, they can cause various problems, including food poisoning and intestinal infections.

The pathogenicity of *Salmonella* is mainly caused by various virulence factors. These virulence factors can help *Salmonella* invade host cells, disrupt the host immune system, and cause intestinal inflammation, etc. Among them, the surface antigens of *Salmonella* can help it adhere to the intestines, invade host cells, and evade attacks from the host immune system. The surface antigens of *Salmonella* include capsules, flagella, O antigens, H antigens, etc. Different combinations of these surface antigens form different strains and serotypes. For example, certain strains of *Salmonella* can evade attacks from the host immune system by changing the combination of capsules. It can also secrete various toxins, including endotoxins, cytotoxins, and exotoxins. These toxins can destroy the structure and function of host cells, causing cell death and tissue damage. The endotoxin of *Salmonella* is a lipopolysaccharide that can cause an inflammatory response in the host immune system, leading to symptoms such as vasodilation and hypotension. Its cytotoxin can destroy the membrane structure of host cells, leading to cell death. For example, *Salmonella* cytolysin is a cytotoxin that can destroy the membrane of host cells. The exotoxin of *Salmonella* can inhibit the signal transduction pathway of the host immune system and disrupt the immune response of host cells (Behnsen et al., 2015).

Salmonella also has various transport proteins, including *Salmonella* pathogenicity island (SPI) 1, SPI-2, etc. These transport proteins can help *Salmonella* enter host cells and evade attacks from the host immune system, thereby causing infections. SPI-1 and SPI-2 are two different transport proteins that play roles in different stages of infection. SPI-1 can help *Salmonella* enter host intestinal epithelial cells, while SPI-2 can help *Salmonella* survive and multiply inside host cells.

2 The Process of *Salmonella* Infection

2.1 The routes and processes of *Salmonella* infection

Salmonella typically survives and reproduces in the intestines of humans and animals. People can contract *Salmonella* by consuming contaminated food or drinking contaminated water. In addition, they can also become infected with this bacterium through contact with animals infected with *Salmonella*, or by directly touching objects contaminated with *Salmonella* (Figure 2).

The process of *Salmonella* infection can be divided into invasion, survival, and reproduction stages. In the invasion stage, *Salmonella* adheres to and invades host cells through intestinal epithelial cells. *Salmonella* utilizes structures such as flagella and capsules on its surface to adhere to and invade host cells. Additionally, *Salmonella* can secrete various toxins, such as *Salmonella* cytolysin, to disrupt the membrane structure of host cells, promoting cell adhesion and invasion (Sahler et al., 2018) (Figure 2).

In the survival stage, *Salmonella* needs to evade attacks from the host immune system to survive in the host body. To achieve this, *Salmonella* can utilize its transport proteins, such as SPI-1, to enter the interior of cells, thereby avoiding attacks from the host immune system. *Salmonella* also secretes various toxins such as endotoxins and cytotoxins to suppress the immune response of the host immune system and reduce inflammation.

In the reproduction stage, *Salmonella* utilizes its transport proteins, such as SPI-2, to acquire nutrients from within host cells, allowing it to reproduce and survive. Additionally, Salmonella secretes various enzymes and proteases to disrupt the structure and function of host cells, promoting its growth and reproduction (Hornef et al., 2002). After reproducing inside the cell for a period of time, *Salmonella* leaves the host cell and further spreads to other host cells or tissues. They escape by disrupting the host cell membrane or are directly phagocytosed by host cells and survive within them.

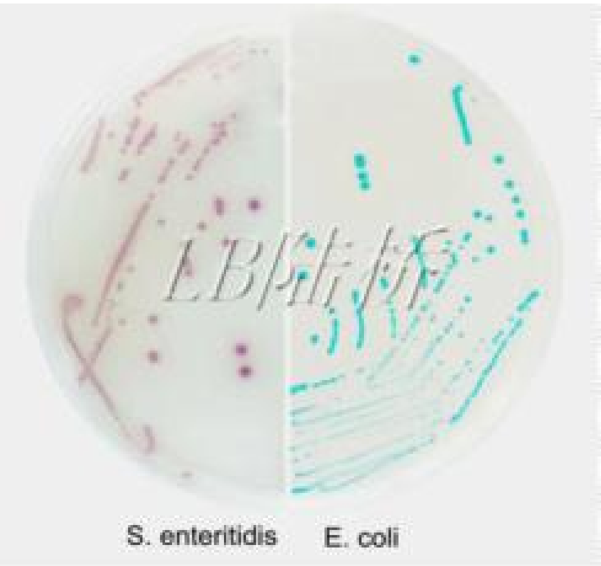

Figure 2 Land Bridge ESM *Salmonella* chromogenic agar (GB 4789.4-2010 Food Microbiology Examination - *Salmonella* Testing)
Note: *Salmonella*: Purple-red colonies; Non-Salmonella: Blue-green, colorless, or inhibited

2.2 The life cycle of *Salmonella* within the host body

The process of *Salmonella* within the host body is quite complex. After infecting the host, *Salmonella* needs to evade the attack of the host immune system to survive within the host. *Salmonella* adheres to the host cell surface using specific structures such as flagella and pili, and further invades the host cell by releasing virulence factors and secreting systems. Once successfully invading the host cell, *Salmonella* begins intracellular replication. It utilizes the nutrients and metabolic mechanisms provided by the host cell to synthesize DNA, RNA, and proteins, and continuously replicates itself through the process of division. In this way, *Salmonella* is able to multiply in large numbers and continue to infect the host.

After reproducing within the cell for a period of time, *Salmonella* leaves the host cell and further spreads to other host cells or tissues. They can escape by disrupting the host cell membrane or be phagocytosed by host cells and survive within them. *Salmonella* also employs several strategies to evade surveillance and attack by the host immune system. Through the action of virulence factors, they interfere with the signal transduction pathway of host cells, reducing the resistance of the host immune system. At the same time, *Salmonella* can also produce various molecules, such as surface proteins and lipopolysaccharides, to activate the inflammatory response of the host immune system, thereby forming inflammatory foci (Sahler et al., 2018).

The survival and reproduction of *Salmonella* within the host are also influenced by the host immune system. When the host immune system senses the presence of *Salmonella*, a series of immune responses will be initiated, such as inflammation, phagocytosis by macrophages, etc. *Salmonella* needs to evade these immune responses in order to survive and multiply within the host. To achieve this, *Salmonella* can utilize its transport proteins, toxins, etc., to evade attacks by the host immune system.

2.3 The host immune response after *Salmonella* infection

After *Salmonella* infection, the host immune system initiates a series of immune responses. The most important of these is the inflammatory response. Inflammation is a protective response of the host immune system that can clear *Salmonella* and other pathogens, and restore the function of damaged tissues. The characteristics of inflammation include redness, swelling, heat, pain, and tissue damage. During the inflammatory response, the host immune system releases a variety of inflammatory cytokines such as TNF-α, IL-1β, and IL-6 to induce inflammation. The inflammatory response involves vasodilation, increased blood flow, and aggregation of white blood cells to direct immune cells and inflammatory mediators to the site of infection to prevent further spread of the pathogen. In addition, immune cells such as macrophages, dendritic cells, and neutrophils are activated, which eliminate the infection by recognizing and destroying *Salmonella*, releasing cytotoxins, and producing cytokines.

In addition to the inflammatory response, the host immune system also initiates a macrophage phagocytic response. Macrophages are important immune cells that can phagocytose and kill *Salmonella* and other pathogens. Macrophages can also release a variety of inflammatory cytokines such as TNF-α, IL-1β, and IL-12 to induce inflammation and promote immune responses.

After *Salmonella* infection, the host immune system also initiates adaptive immune responses. Adaptive immune responses include cellular immunity and humoral immunity. Cellular immunity mainly clears *Salmonella* and other pathogens through T cells and macrophages. Humoral immunity mainly clears *Salmonella* and other pathogens through antibodies. These antibodies can neutralize the virulence factors of *Salmonella*, prevent its invasion into host cells, and promote its phagocytosis and destruction. In addition, cellular immune responses also play an important role, including cell-mediated immune responses and cytotoxic effects. Activated T cells and natural killer cells release cytotoxins that directly cause the death of infected cells. After successfully fighting *Salmonella* infection, the immune system forms immunological memory. This means that the host immune system can quickly recognize and respond to reinfection by rapidly activating immune responses to prevent the reproduction and spread of *Salmonella*.

3 The Interaction of *Salmonella* with the Host Immune System

3.1 The role of *Salmonella* in infecting host cells

Before infecting host cells, *Salmonella* must first adhere to the surface of the host cell. To do this, *Salmonella* can utilize specific proteins on its surface, such as the FimH protein, to bind to receptors on the surface of the host cell, forming a strong connection. This adhesion allows *Salmonella* to more effectively invade the host cell interior.

After *Salmonella* infects the host cell, it enters the interior of the host cell. This process typically relies on

Salmonella's type three secretion system (T3SS). The T3SS injects *Salmonella* proteins directly into the host cell, altering its biological activity. These proteins include those encoded by the pathogenicity island, such as SPI-1 and SPI-2. These proteins help *Salmonella* evade the attack of the host immune system while also acquiring necessary nutrients and growth conditions within the host cell. In addition to invading the host cell interior, *Salmonella* can also interact with host cells in other ways. For example, *Salmonella* can release toxins that disrupt the structure and function of host cells. These toxins include endotoxins, cytotoxins, and hemolysins. These toxins can cause the death of host cells and tissue damage, the

3.2 The impact of *Salmonella* on the host immune system

After *Salmonella* infection, the host immune system initiates a series of immune responses, such as the inflammatory response and adaptive immune response mentioned earlier. However, *Salmonella* can also influence the host immune system in various ways to promote its growth and reproduction.

Salmonella first alters the balance of the host immune system. It can release specific molecules that act as inflammatory cytokines and cause inflammation and tissue damage. Additionally, *Salmonella* can suppress certain components of the host immune system, such as T cells and macrophages, reducing the host's ability to fight the infection. *Salmonella* also interferes with signal transduction in the host immune system. For example, *Salmonella* can release proteins such as SipA and SopB through its T3SS to alter signal transduction pathways in host cells. These proteins can interfere with key molecules in cell signaling pathways, such as Rho GTPase, thereby affecting the biological behavior of host cells. *Salmonella* also exploits the host immune system to promote its own growth and reproduction. For instance, *Salmonella* can regulate the host immune response by releasing molecules such as flagellin and bile acids. Bile acids are compounds found in bile that are released by *Salmonella* upon infection. Flagellin stimulates the production of bile acids by host intestinal epithelial cells. Bile acids can interact with the host's TGR5 receptor to inhibit the inflammatory response of immune cells, thereby helping *Salmonella* evade the host's immune attack (Flynn and Chan, 2003; Raffatellu et al., 2006).

3.3 The immune evasion mechanisms of *Salmonella* against immune responses

Salmonella can evade the attack of the host immune system through various mechanisms. For example, *Salmonella* can alter its surface structure to avoid recognition and attack by the host immune system. *Salmonella* can change the structure of its LPS molecules to evade antibodies and immune cells produced by the host immune system. *Salmonella* also releases molecules that interfere with the function of the host immune system. These proteins can affect the biological behavior of host cells, making it difficult for them to effectively fight *Salmonella* infections. *Salmonella* can also use its T3SS to evade the attack of the host immune system. The T3SS injects *Salmonella* proteins directly into host cells, altering their biological activity. These proteins can help *Salmonella* evade the attack of the host immune system while also acquiring necessary nutrients and growth conditions within the host cell (Arciola et al., 2018).

Salmonella can also interfere with the balance of the host immune system. *Salmonella* can activate the host immune system by releasing specific molecules, such as LPS and flagellin. These molecules stimulate the production of large amounts of inflammatory cytokines, such as TNF-α, IL-1β, IL-6, etc. (Bueno et al., 2007). These inflammatory cytokines cause inflammation and tissue damage, weakening the host's ability to fight the infection and providing a better growth environment for *Salmonella*.

4 Diagnosis and Treatment of *Salmonella* Infection

4.1 Diagnostic methods for *Salmonella* infection

The diagnosis of *Salmonella* infection is achieved by isolating and identifying *Salmonella*. Traditional diagnostic methods include cultivation and biochemical analysis. In these methods, samples are usually collected from biological fluids such as blood, feces, urine, etc. of patients. After processing, the samples are cultured and biochemically analyzed to detect the presence of *Salmonella*. The advantages of these methods are simplicity and ease of operation, but they require a relatively long time and usually take several days to obtain results.

With the development of molecular biology and immunology, modern diagnostic methods have been further improved. For example, PCR technology can rapidly and accurately diagnose *Salmonella* infection by detecting the genes of *Salmonella*. Similarly, immunological methods can also detect the level of *Salmonella* antibodies in patients to determine the presence of *Salmonella* infection.

In addition to traditional diagnostic methods, there are also new technologies being studied, such as mass spectrometry analysis and fluorescence spectroscopy analysis. The advantages of these methods are fast speed, high sensitivity, good specificity, but they still need further validation and application. Currently, the diagnosis of *Salmonella* infection is constantly developing and improving. Although traditional diagnostic methods remain important diagnostic tools, the development of modern technology will provide more choices and more efficient methods for the diagnosis of *Salmonella* infection.

4.2 Treatment methods for *Salmonella* infection

The treatment methods for *Salmonella* infection mainly include antibiotic therapy and supportive care. Currently, commonly used antibiotics include fluoroquinolones, cephalosporins, aminoglycosides, and macrolides. These antibiotics can treat *Salmonella* infection by inhibiting the growth and reproduction of *Salmonella*. The choice of antibiotics should be based on the drug sensitivity of *Salmonella* and the clinical condition of the patient (Figure 3). During treatment, adjustments and monitoring should be made based on the patient's condition and adverse drug reactions.

Figure 3 *Salmonella* detection and culture (GB 4789.4-2010 Food Microbiology Examination - Salmonella Testing)

Besides antibiotic therapy, supportive care is also an important treatment for *Salmonella* infection. Supportive care plays an important role in the treatment of *Salmonella* infection. *Salmonella* is a type of bacteria that can cause food poisoning or *Salmonella* infection, usually manifesting as symptoms such as diarrhea, fever, and vomiting. In addition to drug treatment targeting the pathogen, supportive care is one of the key methods to help patients relieve symptoms and promote recovery. Supportive care includes maintaining water and electrolyte balance, correcting malnutrition, and managing symptoms. For example, diarrhea and vomiting can lead to fluid loss and cause dehydration and electrolyte disorder，so providing sufficient fluids and appropriate electrolyte supplements can help maintain balance in the body. *Salmonella* infection may affect appetite and lead to inadequate nutritional intake. Therefore, providing easily digestible foods and maintaining adequate nutritional intake can help accelerate recovery. Additionally, appropriate medications can help relieve pain and fever, improving patient comfort. During the infection period, proper isolation and rest can help the body fully resist the infection and promote recovery. During treatment, the patient's condition and vital signs should be closely monitored, and complications should be corrected and managed in a timely manner (Wang et al., 2020).

In recent years, some new treatment methods are being studied, such as vaccines and immunotherapy. Vaccines can prevent *Salmonella* infection by stimulating the immune response of the body. Currently, there are some

Salmonella vaccines that have been applied in clinical practice. Immunotherapy can enhance resistance to *Salmonella* by boosting the immune function of the body. These new treatment methods still need further research and validation.

Although the treatment methods for *Salmonella* infection are constantly developing and improving, antibiotic therapy and supportive care remain the main treatment methods. With the development of technology and further research, there will be more treatment methods available to provide more options and more efficient methods for the treatment of *Salmonella* infection.

4.3 The prevention and control of *Salmonella* infection

Salmonella infection is a common food-borne illness that is mainly transmitted through contaminated food or drinking water. Therefore, the key to preventing *Salmonella* infection is strengthening food safety management and personal hygiene.

In terms of food safety management, it is necessary to strengthen the supervision of food production and sales to ensure that food meets standards and regulations. Food producers and sellers should follow the corresponding hygiene standards and operating procedures to ensure the hygienic safety of food. Consumers should choose safe and reliable food and pay attention to the preservation and cooking methods of food.

In terms of personal hygiene, attention should be paid to the cultivation of personal hygiene habits. Frequent handwashing should be done to avoid contact with pollutants and pathogens. Hands must be washed before and after handling food, and clean tools and disinfectants should be used to maintain food hygiene. During travel and outdoor activities, hygiene standards and regulations should be followed to avoid drinking contaminated water and eating untreated food.

Vaccination is also an effective means of preventing *Salmonella* infection. Currently, some *Salmonella* vaccines have been applied in clinical practice. People at high risk, such as farmers, animal breeders, food processors, etc., should receive the corresponding vaccine to prevent *Salmonella* infection.

5 Summary and Outlook

This study reviewed the diagnosis, treatment, prevention and control methods of *Salmonella* infection, and explored their progress and future trends. The aim is to enhance the understanding of *Salmonella* infection, prevent and control *Salmonella* infection, and reduce the occurrence and transmission of *Salmonella* infection. In terms of the diagnosis of *Salmonella* infection, the study mentioned traditional diagnostic methods and modern diagnostic methods. In traditional methods, culture and biochemical analysis are commonly used methods. Although these methods are simple and easy to perform, they require a long time. Modern diagnostic methods include PCR technology and immunological methods, which can diagnose *Salmonella* infection quickly and accurately. It is believed that more diagnostic methods will be applied, providing more choices and more efficient methods for the diagnosis of *Salmonella* infection. In addition, new treatment methods such as vaccines and immunotherapy are being studied.

With the development of technology and the deepening of research, more treatment methods will be applied, providing more choices and more efficient methods for the treatment of *Salmonella* infection. For the prevention and control of Salmonella infection, it is necessary to strengthen food safety management and personal hygiene habits. In addition, vaccination is also an effective means of preventing *Salmonella* infection.

As a common disease, *Salmonella* infection has a significant impact on human health. Therefore, it is necessary to strengthen the understanding of *Salmonella* infection, prevent and control the occurrence and transmission of *Salmonella* infection. In the future, research on the mechanism of *Salmonella* infection, the development and application of *Salmonella* vaccines, and epidemiological studies on *Salmonella* infection can effectively prevent and control the occurrence and transmission of *Salmonella* infection, making greater contributions to human health.

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