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EPIDEMIOLOGICAL FEATURES AND APPLICATION OF TYPHOID VACCINE

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Abstract: Typhoid fever is still widespread and dangerous in low- and middle-income countries. Antibiotics are commonly used for treatment, but endemic countries have experienced problems with drug-resistant strains, making treatment time-consuming and expensive. Salmonella enterica, the causative agent of typhoid fever (S. typhi), remains a problem in many low- and middle-income countries. In industrialized countries, improved sanitation and food hygiene has been an effective means of fighting diseases. However, in most of the affected regions, this progress has been limited by slow socio-economic progress. As a result, vaccination is an effective means of preventing the disease in both the short and medium term. The oral typhoid vaccine and the Vi polysaccharide typhoid vaccine have been available for a long time, but most of the population, especially infants and children under the age of two, are still at risk. Efforts to prevent typhoid fever have recently increased thanks to conjugated vaccines based on Vi polysaccharides and funding to support vaccination by the Gavi Alliance. The supply of the vaccine will be crucial, and numerous efforts are being made to provide new typhoid vaccines to populations in dire need. This review provides an overview of licensed typhoid vaccines, as well as potential vaccines that are currently under development, as well as prospects for their implementation.

Keywords: S. Enterica, S. Typhi, immunogenicity, conjugated typhoid vaccines, antimicrobial resistance, epidemiology.

Introduction. Typhoid fever, also known as typhus abdominalis, is an acute anthroponotic infectious disease caused by S. Enterica Typhi serotype. The patient has fever, symptoms of general intoxication, bacteremia, ulcerative lesions of the lymphatic system, mainly in the small intestine, and hepatolienal syndrome. Despite the fact that typhoid fever is spreading all over the world, most people get sick in areas with poor water supply and sanitation. The consumption by the population of epidemic-poor drinking water with unsatisfactory or insufficient sewerage of the territory leads to high activity of the transmission waterway, which causes acute and chronic water outbreaks/epidemics and the spread of typhoid fever. Neutralization of the activity of the transmission waterway leads to a natural decrease in morbidity to a sporadic level or even to a complete absence in some areas [1-4]. A human (patient, convalescent, or bacterial carrier) is the only natural source and reservoir of S. Typhi. The main role in the spread of S. Typhi belongs to chronic bacterial carriers. Infection occurs through faeces and mouth. Infections can spread through water, food and household contact routes. Among them, the waterway is of particular importance. The peak incidence of typhoid fever occurs mainly in summer and autumn. The sporadic incidence does not depend on the season. The natural susceptibility of the population is high; from 40 to 50% of the population can get sick in epidemic foci. Currently, there are more and more new strains resistant to various antibiotics. 10-18% of typhoid fever patients develop complications. Infectious-toxic encephalopathy, infectious-toxic shock, intestinal bleeding, intestinal perforation and rupture of the spleen are all complications that require immediate medical intervention. The mortality rate ranges from 60 to 100 percent in severe cases. WHO estimates that 11-20 million people get typhoid fever a year and from 128 to 161 thousand people die from it. Over the past few

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decades, the incidence of typhoid fever has decreased significantly in industrialized countries. Nevertheless, in some countries of the former USSR, in south and east Asia, Africa and South America, typhoid fever continues to be a serious public health problem. Bacterial carriers and the main sources of infection are common in places where they are common [5-11]. The main route of S. typhi spread is fecal-oral, through contaminated food and water. Therefore, the best methods of preventing and controlling typhoid fever include providing safe water, improving sanitation and hygiene. Given the growing evidence of the global burden of typhoid fever, especially among young children, and the long-term prospects for sustainable and effective improvement of water supply and sanitation in low-income countries, there is a growing consensus in favor of paying special attention to preventive vaccination [12, 13, 14].

The main purpose of this publication is to conduct a short literature review on the epidemiological features and application of the typhoid vaccine

Epidemiological features of typhoid fever Humans are the only natural source and reservoir of S. Typhi. The main factor contributing to the spread of S. Typhi is chronic bacterial carriers, especially in places of public catering and trade, water supply, children's institutions and other places that are important for the spread of infection. The pathogen S.Typhi causes the disease in 25% of artificially infected adults. This pathogen contains 10 or 100,000 microbial cells in only 0.001-0.01 g of feces of a chronic bacterium excretory agent and a patient with typhoid fever. A few dozen or a thousand microbial cells did not cause diseases. A person who has been infected secretes millions of viable typhoid bacilli in feces, urine and bile. S. Typhi secretes the largest amount with feces during 1-5 weeks of the disease, with a maximum at week 3, and with urine for up to 4 weeks. Convalescents often release the pathogen to the outside world within 14 days for transient carriage, in 10% of those who are ill, this lasts up to 3 months for acute carriage, and 3-5% become permanent carriers of S. Typhi for a number of years. When the release of S. Typhi is discrete, rather than constant, the so-called intermittent carrier is possible in chronic bacterial isolators. This increases their epidemiological danger. Infected shellfish or oysters in contaminated water may be the source of S.Typhi. Flies contaminate foods where microorganisms can multiply and reach an infecting concentration. Infection occurs through faeces and mouth [15-19].

The infection can spread in the following ways: aquatic (the pathogen enters the human body through the use of infected water); food (the pathogen enters the human body through the use of contaminated food or milk); contact and household (the pathogen can spread through contaminated hands and household items). He is a leader in institutions where patients stay around the clock. The peak incidence of typhoid fever occurs mainly in summer and autumn. The sporadic incidence does not depend on the season. The natural susceptibility of the population is high; up to 40%- 50% of the population can get sick in epidemic foci. The immune system in typhoid fever is non-sterile, long-lasting and nonspecific. Recurrent typhoid fever can occur after a long period of time after the first disease or when a high infectious dose of S. Typhi is injected into the body. In addition, repeated cases of typhoid fever have been reported after a relatively short period of time (1.5-2 years), which is associated with impaired immunogenesis as a result of antibiotic therapy [20-24].

The peculiarities of the current course of typhoid fever are associated with the more frequent use of antibacterial drugs and vaccination against typhoid fever. Mild cases have become more frequent, when general intoxication is weak and many typical symptoms are absent. Even without the use of AMP, the feverish state lasts up to seven days. Lymphadenopathy manifests itself in 60-80% of cases when the onset of typhoid fever is acute. Atypically current cases, such as typhoid fever, present difficulties in diagnosis because they have symptoms of acute gastroenteritis and short-term fever that lasts up to three days. Perforation of an intestinal ulcer can occur during the period of convalescence at normal body temperature. and the results of laboratory tests. Almost half of the patients retain

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eosinophils in the blood and normocytosis is observed. Serological reactions may remain negative throughout the disease [25-27].

An increase in body temperature is usually accompanied by chills, which are often repeated. The fever grows rapidly and reaches a maximum after 1-2 days. From the very beginning, patients experience severe general weakness, headache, mainly in the forehead, dry mouth, severe hunger, myalgia and arthralgia in the lower extremities, as well as intestinal dysfunction. The stool is liquid, light brown or greenish in color, without pathological impurities, stools up to 3-4 times a day. Rhinitis and pharyngitis often occur. The patient's face may be hyperemic in the first days of the disease, and then becomes pale. At first, the pulse is frequent, and only at the beginning of the disease it becomes normal. A brown plaque forms quickly on the tongue. Bleeding cracks form on it if the necessary preventive measures are not taken [28-31].

Relapses of typhoid fever are more common after widespread use of AMP. Pneumotif, meningotif, encephalotif, colotif, appendicotif, cholangotif and nephrotif are rare forms. Symptoms typical of lesions of a particular organ dominate the clinical picture. Serum antitoxic substances neutralize toxins released by typhoid bacteria during their life cycle. Thus, there are almost no symptoms of intoxication. In some patients, a thorough examination reveals concomitant diseases of the liver and biliary tract, most often chronic hepatocholecystitis and cholangitis. The functional state of the liver is preserved: cholesterol synthesis, lactate dehydrogenase and other processes are disrupted. There are hypoacid and achilic symptoms, which at first may be the only sign of gastrointestinal damage [32-35].

The types of bacterial carrier are classified as follows: Prolonged spread of bacteria (the release of S.Typhi persists for the first three months after typhoid fever);

chronic infection with bacteria, for example, when S.Typhi is released after typhoid fever for more than three months. Discharge (decompensation) and latency (compensation) are two stages of chronic bacterial transmission.

The transient spread of bacteria is very rare. It can only be detected in the immune system of previously vaccinated people under the following conditions: a) communication with a patient with typhoid fever or paratyphoid A and B; b) detection only in coproculture; c) absence of typhoparathyphoid or any febrile disease in the anamnesis during the last three months; and d) negative results of bacteriological studies of urine, blood, bone marrow, bile and serological Antibacterial drugs can cause a phase of latency in long-term bacterial carrier [36-40].

Treatment of typhoid fever: According to clinical and epidemic indications, every patient with typhoid fever should be hospitalized in an infectious hospital. Patients are hospitalized within the first three hours, and in rural areas within six hours after receiving an emergency message. In areas where typhoid fever is common, outpatient hospitalization is required for people with a febrile condition that lasts more than three days and requires mandatory blood testing for hemoculture. Patients who have just returned are placed separately from the convalescents. Treatment depends on how severe the disease is and how long it lasts. Treatment depends on how severe the disease is and how long it lasts. Treatment of patients with typhoid fever should be comprehensive and carried out in several directions: protection; careful hygienic care of patients in serious condition; nutrition; exposure to the pathogen; detoxification and restoration of homeostasis; restoration of water-electrolyte balance (if necessary); elimination of structural and functional changes in the gastrointestinal tract; and the restoration of normal condition [41-44].

Prevention: General methods of typhoid fever prevention are regulated, and specific typhoid fever prevention is carried out in accordance with epidemiological indications and taking into account the sanitary and communal provision of settlements, morbidity levels and the epidemiological situation. Preventive immunization of the population is carried out in the following cases: 1. in areas where the

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incidence exceeds 25 cases per 100 thousand people; 2. among adults who are at risk: employees of municipal landscaping, enterprises for the collection, transportation and disposal of household waste; people working with live cultures of typhoid fever; employees of infectious diseases hospitals and departments where patients with intestinal infections are treated; and others. Extreme conditions, such as military conflicts, earthquakes, floods and others, cause mass migration of the population and accommodation in camps for displaced persons (refugees) and temporary shelters. When there is a threat of epidemics and outbreaks, such as natural disasters, major accidents on water and sewer networks, vaccinations are also carried out according to epidemiological indications. The population should be vaccinated 1-2 months before the start of the seasonal increase in the incidence of typhoid fever 3% [45-50].

Discussion. The causes of typhoid fever have been known for more than a hundred years, but this disease, which is usually moderate or severe and sometimes recurrent, still poses a serious threat to global health. In cases where non-specific prevention is not available or antimicrobial therapy is ineffective due to the growing antibiotic resistance of the pathogen, vaccination may be the most effective method of preventing infectious diseases. A study of the current state and trends in the development of typhoid vaccine prophylaxis has shown significant progress in vaccination of various population groups, including children under two years of age. The European Recommendation does not respect unity. Current country-specific recommendations should be the basis for evaluating travelers' vaccination. Doctors working on trips should be aware of the problems associated with vaccinating travelers and are motivated to raise awareness about the risks of typhoid and paratyphoid. Many of the developed vaccines have passed all licensing stages and are now available for purchase worldwide. Improving the effectiveness of previously developed vaccines and the development of new combined vaccines against typhoid fever remain the main directions of modern vaccinology due to the high epidemiological significance of the disease [51-55].

The main methods of combating typhoid fever are improved diagnosis with a high degree of clinical suspicion, better diagnostic studies, early and accurate detection of resistance, treatment with appropriate medicines, improved hygiene and sanitation, including the provision of safe drinking water in endemic areas and vaccination of both travelers and local populations. Although typhoid vaccines are recommended for travelers traveling to areas at risk, it should be borne in mind that they are moderately effective and cannot protect against salmonella paratyphs. Improved vaccines against salmonellosis typhoid and paratyphoid A are required [55-60].

In countries with high disease burden or significant antimicrobial resistance, the introduction of an effective single dose of typhoid vaccine can have a significant impact by protecting children from infection, reducing the use of antimicrobials and related health inequalities in the poorest regions of the world [61-65].

Conclusion. Over the past hundred years, preventive vaccination has significantly reduced morbidity and mortality from infectious diseases around the world. This process is regulated by national routine vaccination schedules. All children should be able to realize their full potential in health and well-being, and no child should die from preventable causes [66, 67].

Thus, typhoid fever remains the main cause of morbidity and mortality in low- and middle-income countries, indicating a significant burden among children. In the world, typhoid and paratyphoid are common among children under the age of two, whose symptoms are as severe as in older children [68].

Broader efforts are needed to reduce the burden of paratyphoid, but early vaccination with conjugated typhoid vaccines can prevent significant morbidity. Despite the evidence of the high effectiveness of vaccination within the framework of a routine immunization program over the past decades, typhoid

and paratyphoid fever requires urgent improvement, taking into account current trends in the development of vaccination. The supply of the vaccine will be crucial, and numerous efforts are being made to ensure that new typhoid vaccines are available to populations in dire need [69].

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