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Research Article

Current Status and Research Progress of Chinese Children's Immunization During The COVID-19 the Pandemic Situation

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Abstract

Vaccination is the most economical and effective means to prevent control and even eliminate infectious diseases, and it is one of the most basic public health service items provided by the government to the masses. Every year, April 25th is the Publicity Day for Children's Vaccination in China. Due to the new crown pneumonia, the city is closed to fight the epidemic, and the vaccination is suspended. My country's rapid control of the new crown epidemic has started in an orderly manner with child vaccinations. In the 70 years since the founding of New China, my country's public health, especially the prevention and control of infectious diseases, has made world-renowned achievements, which are inseparable from vaccination. This article aims to carry out the vaccination work under the prevention and control of the epidemic situation in my country, the types of domestic Class I and II vaccines and the vaccination procedures, as well as the methods for replanting children after they are not vaccinated in time due to the epidemic or other uncontrollable factors. Vaccine research and application development of innovative vaccines are summarized and sorted out.

Overview

Vaccination is the most economical and effective means to prevent control and even eliminate infectious diseases, and it is one of the most basic public health service items provided by the government to the masses. The popularity of childhood immunization has reduced the incidence of vaccine-preventable diseases nationwide to the lowest level in history [1]. Every April 25th is the Publicity Day for Children's Vaccination in China. Due to the new crown pneumonia, the city is closed to fight the epidemic, and the vaccination has to be announced for a while. There are many epidemics, but anti-epidemic is as important as vaccination and cannot be delayed. Vaccination is also an important measure and method to prevent infectious diseases in children. Fortunately, due to the rapid control of the epidemic in our country, the current child vaccination work has gradually resumed. Data collected by WHO, UNICEF, and the Global Alliance for Vaccines and Immunization indicate that due to the COVID-19 pandemic, at least 80 million children under the age of one may not be routinely vaccinated, affecting at least 68 countries to stop routine vaccinations. Dr. Tedros Adhanom Ghebreyesus, Director-General of the World Health Organization, said in a press release: "Immunization is one of the most powerful and basic disease prevention tools in the history of public health." The destruction may undermine decades of progress in vaccine-preventable diseases such as measles." According to the news released, dozens of countries have postponed the targeting of polio, meningitis, yellow fever, typhoid fever, cholera, and tetanus. Moreover, vaccination campaigns against measles, mumps and rubella. UNICEF Executive Director Henrietta H. Fore said in a press release: "We cannot allow our efforts to fight one disease at the expense of our long-term progress in fighting other diseases." We have effective vaccines against measles, polio, and cholera. Although circumstances may require us to temporarily halt certain rabbit disease efforts, these immunizations must be restarted as soon as possible, otherwise we may turn a deadly epidemic into another Field" [2].

Meaning

The practice of preventing diseases through immunization in the world first originated in China. In 1727, Yu Maokun's "Golden Mirror Fu Jijie" of the Pox Branch records that during the Ming Longqing period (1567 ~ 1572), Taiping County, Anhui first created the method of vaccination. In 1962, the Ministry of Health issued the "Measures for Vaccination", and in 1963 the "Implementation Measures for Vaccination Work". Four kinds of vaccines (BCG, polio candy, diphtheria, and measles) were administered to immunized subjects in large cities. Timely vaccination, in rural areas, winter and spring surprise vaccination is mainly carried out. In the early 1960s, my country eliminated smallpox through vaccinia vaccination, more than 10 years before the World Health Organization (WHO) announced the global eradication of smallpox in 1980. In 2000, my country successfully eliminated polio and has maintained a polio-free state until now [3]. In 2012, my country eliminated neonatal tetanus. The measles, meningitis, Japanese encephalitis, diphtheria and other serious vaccines that have been raging in history can prevent infectious diseases, and the incidence has now dropped to the lowest level in history [4]. The mother-to-child transmission of hepatitis B was cut off from the source by vaccinating newborns with hepatitis B vaccine. The hepatitis B surface antigen-carrying rate of children under 5 years of age has dropped from 9.67% in 1992 to 0.32% in 2014. The prevention and control of hepatitis B in China has been praised by the WHO as "21 A great achievement in the field of public health in the century" [5]. In 1978, my country launched the immunization program in an all-round way, continuously increasing the types of vaccines in the immunization program, from the original four vaccines to prevent six diseases to five vaccines to prevent seven diseases. In 2008, my country implemented the expanded immunization program project, which included vaccines that can prevent 12 diseases in children into the national immunization program. My country has gradually achieved the goal of achieving a vaccination rate of over 85% in the immunization program based on provinces, counties, and townships. At present, China's CDC has also established a national immunization program technical working group to provide technical support for NIAC, marking my country's immunization program. Planning and issuing policymaking has taken another big step forward in evidence-based

decision-making. The "Vaccine Management Law of the People's Republic of China" implemented at the end of 2019 implements the "four strictest" spirit from the entire process of vaccine production, distribution and vaccination, and further enhances the confidence and safety of vaccination [6].

Situation and Classification of Vaccines for Children in China

China's childhood vaccine situation

Because China's national conditions are different from those of European and American countries, foreign vaccine guidelines cannot be directly applied in China. For example, compared with the formaldehyde inactivated hepatitis A virus vaccine used in most countries, more immunogenic self-developed live attenuated vaccines are used in China (Table 1) [7-8], Japanese encephalitis (Japanese encephalitis) virus has a low incidence in Europe, America, Australia, and other places and does not require extensive vaccine protection. Therefore, countries in Europe and the United States have not included this vaccine in their routine plans. Due to the high risk of transmission of the disease, China will It is included in the Class I plan for vaccine protection, and is different from the inactivated vaccines commonly used in developed countries. The live attenuated vaccine is widely used in China [9].

Note: DTaP-Hib：Diphtheria, tetanus, acellular pertussis, Haemophilus influenzae type b mixed vaccine；DTaP-Hib-IPV：Diphtheria, tetanus, acellular pertussis, Haemophilus influenzae type b, inactivated polio vaccine

Table 1: Major types of vaccines in China.

Type of Caccine		Vaccine Name
Live attenuated vaccine		MMR vaccine and the corresponding double and single vaccine, Japanese encephalitis live attenuated vaccine, Live attenuated hepatitis A vaccine, Oral live attenuated polio vaccine, 5-valent rotavirus vaccine, Chickenpox Vaccine, BCG vaccine (contains live BCG cells)
Inactivated vaccine	Whole virus vaccine	Inactivated polio vaccine, inactivated Japanese encephalitis vaccine, inactivated hepatitis A vaccine, inactivated enterovirus 71 (EV71) vaccine, inactivated influenza virus vaccine, rabies vaccine
Component vaccine	Toxin protein	DPT vaccine and DPT vaccine, hepatitis B recombinant vaccine, influenza virus split vaccine, human papilloma virus-like particle vaccine
	Polysaccharide antigen	Group A meningococcal meningitis (referred to as meningitis) polysaccharide vaccine, Group A and C polysaccharide vaccine, ACYW35 polysaccharide vaccine, 23-valent streptococcus pneumoniae polysaccharide vaccine
	Polysaccharide antigen binding protein	Meningococcal A+C conjugate vaccine, 13-valent Streptococcus pneumoniae conjugate vaccine, Haemophilus influenzae type b conjugate vaccine
Other vaccines		DPT-based combined vaccine: DTaP-Hib, DTaP-Hib-IPV

Classification of childhood vaccines in China

Children's vaccines in my country are currently classified into two categories. One is the vaccine within the immunization plan, also known as the I vaccine. It is included in the planned immunization according to the national regulations and is a free vaccine. It is required by the country after the baby is born; unplanned immunization vaccines, also known as Class II vaccines, are self-funded vaccines, which can be determined according to the baby's own situation, the different conditions of each region, and the financial status of the parents (Table 2) [10].

Table 2: Chinese children's immunization schedule and non-immunization schedule vaccines.

Within the Immunization Plan (Free)	Non-Immunization Plan (Paid)
BCG, hepatitis B recombinant vaccine, oral live attenuated polio vaccine, inactivated polio vaccine, DPT vaccine and DPT vaccine, group A meningococcal polysaccharide vaccine, mumps vaccine, Japanese encephalitis reduced Live virus vaccine, live attenuated hepatitis A vaccine, group A and C meningococcal polysaccharide vaccine	5-valent rotavirus vaccine, 13-valent Streptococcus pneumoniae conjugate vaccine, Haemophilus influenzae type b conjugate vaccine, DTaP-Hib, DTaP-Hib-IPV, inactivated polio vaccine , Meningococcal A+C conjugate vaccine, Enterovirus 71 (EV71) inactivated vaccine, Japanese encephalitis inactivated vaccine, varicella vaccine, hepatitis A inactivated vaccine, influenza whole virus inactivated vaccine, influenza virus split vaccine , ACYW35 meningococcal polysaccharide vaccine, 23-valent pneumococcal polysaccharide vaccine, human papilloma virus-like particle vaccine

Specific situation of vaccines in China's childhood immunization program

BCG vaccine

BCG vaccine was invented in the early 20th century by two French bacteriologists, Leon Calmette and Camile Guerin. The inoculation of BCG vaccine in China began in 1933 and was introduced by Dr. Wang Liang from France. He established China's first BCG vaccine laboratory in Chongqing, which opened the way for the research and cultivation of BCG vaccine in China [11]. The annual number of deaths from tuberculosis is 2 to 3 million adults and 100,000 children. BCG is one of the earliest vaccines used in the world. At present, the incidence rate of tuberculosis in my country is about 61/100,000, which is generally a low-incidence country. However, my country has a vast territory, and the incidence rate varies greatly among regions, with high areas above 200/100,000 and low areas It is below 30/100,000, but my country is a country with a rapid decline in the incidence rate, which is also attributed to the BCG vaccination [12]. My country has formally proposed the concept of planned immunization since 1978, and incorporated BCG vaccine into the planned immunization. The vaccination procedure of BCG vaccine in my country is within 24 hours of birth. If not vaccinated in time, people younger than 3 months of age can directly replant. Children between 3 months and 3 years of age are resistant to tuberculin pure protein derivatives (TB-PPD) or BCG Those whose protein derivative (BCG-PPD) test is negative should be replanted, children over 4 years old should not be replanted.

Hepatitis B vaccine

Hepatitis B is caused by the pathogen of hepatitis B virus (HBV). It is mainly an inflammatory disease of the liver and can cause multiple organ damages. An infectious disease seriously endangers human health. Hepatitis B is widely prevalent in countries around the world. There is no certain epidemic period. It can be onset throughout the year. It mainly affects children and young adults. Some patients transform into cirrhosis or liver cancer. Hepatitis B is one of the three major chronic diseases in the world. There are about 350 million hepatitis B carriers in the world, and my country is a high-risk area for hepatitis B. There are more than 100 million hepatitis B virus carriers in my country, accounting for about 10% of our population. Accounting for more than 50% of the world's hepatitis B virus carriers. In 1991, the Ministry of Health promulgated the "National Implementation Procedures for Hepatitis B Vaccine Immunization", which included the hepatitis B vaccine into the management of planned immunization. The domestic hepatitis B vaccine was developed in 1975. The developer Tao Qimin was the first director of the Institute of Liver Diseases, Peking University People's Hospital. The first-generation hepatitis B vaccine was a blood-derived vaccine. Due to its limited production capacity, genetically engineered recombinant vaccines that adopt new technologies and are safer and more effective gradually replaced it. Since January 1, 1992, hepatitis B vaccination has been promoted nationwide, and the blood-derived hepatitis B vaccine has been used until the end of 2000. After 2001, all genetic engineering hepatitis B vaccines have been used [13]. My country's hepatitis B immunization program has three doses: 0, 1, and 6 months old. If the vaccination is not timely within 24 hours after birth, the first dose of vaccination will be arranged first. For children born to mothers with positive hepatitis B surface antigen, the second and third doses of hepatitis B vaccine should also be vaccinated in time. When replanting, the interval between the first and second doses is ≥28 days, the dose of the second and third doses interval should be ≥60 days.

Polio vaccine

Poliomyelitis (referred to as polio) is an acute intestinal infectious disease that is caused by poliovirus types II, III, and I and is mainly transmitted from person to person through the fecal-oral route. After infection, some patients may develop flaccid paralysis, while leaving irreversible sequelae of lifelong paralysis. Vaccination is the safest, effective and economical means to prevent, control and eliminate the disease. My country has included polio vaccine in its planned immunization since 1978. In my country, two doses of inactivated polio vaccine (IPV) and two doses of type I+III live attenuated polio vaccine (type I+III, bOPV) are currently used in combination with sequential immunization [14]. Our country's polio vaccination program has four doses: 2, 3, 4 months old and 4 years old. The principle of replanting: children under 4 years old who have not reached three doses should complete 3 doses, and children ≥4 years old who have reached 4 doses should complete 4 doses. When replanting, follow the immunization procedure of inoculating inactivated polio vaccine first and then live attenuated polio vaccine. The interval between the first 3 doses is ≥28 days.

Diphtheria-pertussis-tetanus vaccine

Whooping cough is a highly infectious disease caused by Bordetella pertussis [15]. Since the 1990s, despite the high coverage of pertussis vaccination, pertussis recurrences have continued to occur in some countries, and the incidence and local outbreaks have increased significantly. Adolescents and adults have significantly increased pertussis cases and have become infants and young children. The main source of infection [16]. After China included the DTP vaccine (DTaP) in its immunization program in 1973 [17], the prevention and control of whooping cough has achieved remarkable results. The average annual incidence of pertussis has decreased from 100/100,000 in the 1960s before the implementation of the immunization program, and 200/100,000 in the 1970s, to 1/100,000 after the implementation of the immunization program [18-19]. Diphtheria vaccine, which is prepared by pertussis vaccine, refined diphtheria and tetanus toxoid in an appropriate proportion, used to prevent three diseases of whooping cough, diphtheria and tetanus. Pertussis vaccine is composed of pertussis vaccine and tetanus toxoid. Adsorbed acellular pertussis vaccine, diphtheria and tetanus-as if mixed vaccine (adsorbed acellular pertussis) currently used in my country. The immunization program of DTP in my country has 4 doses: 3, 4, 5 months old and 18 months old; DTP is 1 dose: 6 years old. Principles of replanting: Children aged 3 months to 5 years old who have not completed the DPT vaccine should use DPT vaccine to make up 4 doses. The interval between the first 3 doses is ≥28 days. The vaccination of the fourth and third doses interval is ≥6 months. For children ≥6 years old who have received DTP and the cumulative total of <3 doses of DTP, use DTP (child type) for 3 supplements from 6 to 11 years old, and use DTP (adults and adolescents) with 3 supplements for children ≥12 years old. The interval between the second dose and the first dose is 1 to 2 months, and the interval between the third dose and the second dose is 6 to 12 months.

Meningococcal vaccine

Epidemic cerebrospinal meningitis is an acute purulent meningitis spread through the respiratory tract caused by infection with Neisseria meningitidis, referred to as meningitis [20], and its mortality rate is 10%-15%, and cured patients are prone to long-term Sequelae. Neisseria meningitidis is a common bacterial meningitis pathogen in the world. According to its surface specific polysaccharide antigens, it can be divided into A, B, C, D, I, K, L13, W135 Among subgroups such as, X, Y, Z, 29E, group A is the main prevalent bacterial group in my country. In recent years, the incidence of group C meningococcal disease has gradually increased, and group C meningococcal meningitis has spread or broke out in local areas [21]. At present, my country's meningococcal vaccine (Men V) has polysaccharide vaccines (MPV) and conjugate vaccines (MCV). Among them, two doses of meningococcal polysaccharide vaccine (MPV-A) of group A and meningococcal polysaccharide vaccine of group A and C (MPV-AC) Two doses of vaccine have been included in the National Immunization Program [22]. My country's meningococcal immunization program has a total of 4 doses: 2 doses for group A meningococcal meningitis at 6 and 9 months old; 2 doses for group A and group C meningococcal meningococcal at 3 and 6 years old. Principles of replanting: Group A meningococcal polysaccharide vaccination has not been completed. Children less than 24 months old should receive two supplements of group A meningococcal polysaccharide vaccine. The interval between the two doses is ≥3 months; children ≥24 months of age should use group A and group C. Make up two doses of EPC vaccine, and the interval between the two doses is ≥3 years, and no more supplements of Group A meningococcal polysaccharide vaccine. The interval between the first dose of group A group C meningococcal polysaccharide vaccine and the second dose of group A meningococcal polysaccharide vaccine is ≥ 12 months.

Japanese encephalitis vaccine

Also known as Japanese encephalitis (Japanese encephalitis for short) in my country, it is an acute central nervous system infectious disease caused by Japanese encephalitis virus (JEV). The clinical symptoms are mainly high fever, convulsions, disturbance of consciousness and meningeal irritation. The case fatality rate can reach 10%, and about 15% of survivors have sequelae. In 2010, the number of cases and deaths of Class A and B statutory infectious diseases reported by the Ministry of Health of my country was ranked 15th and 7th respectively [23], which seriously threatened people's lives and health. At present, there are two types of Japanese encephalitis vaccines: inactivated vaccines and live attenuated vaccines. In 2007, my country included the live attenuated Japanese encephalitis vaccines into the immunization program. Inactivated Japanese encephalitis vaccines belong to category II self-funded vaccines. The immunization program of live attenuated Japanese encephalitis vaccine in my country has 2 doses: 8 months old and 2 years old. Principles of replanting: If the Japanese encephalitis vaccine has not been inoculated, if a live attenuated Japanese encephalitis vaccine is used for replanting, two doses should be made up, and the interval between the two doses should be ≥12 months. Make up 4 doses. The interval between the first and second doses is 7 to 10 days, the interval between the second and third doses is 1 to 12 months, and the interval between the third and fourth doses is ≥3 years.

Measles-rubella-mumps vaccine

Measles, mumps, and rubella are highly contagious viral diseases spread through the respiratory tract. Among them, measles can cause high fever and skin rash, and cause blindness, encephalitis or death. Mumps virus can cause parotid gland inflammation, fever, headache and muscle aches, and can cause serious complications such as viral meningitis. Rubella is usually mild in children, but it can cause fetal death or congenital rubella syndrome in early pregnancy, which can lead to serious birth defects of the brain, heart, eyes and ears. As children are extremely susceptible groups, infection with measles, mumps, and rubella can have serious consequences, but the best way around the world is to prevent the occurrence of the three diseases by vaccination against measles, mumps, and rubella. It is recommended that all countries should plan for comprehensive coverage of measles immunization and adopt combined vaccines such as leprosy (MR), measles (MMR) or measles and varicella (MMRV) to prevent the occurrence of corresponding diseases at the same time [24-25]. As early as 1965, my country had begun to vaccinate against measles and a live attenuated triple vaccine against measles and mumps replaced the vaccine currently included in the immunization program. The immunization program of the live attenuated MMR vaccine in my country is two doses: 8 months old and 18 months old. For children who have reached the age of 8 months and 18 months of age, the MMR vaccine should be arranged first. Children >24 months of age who have not completed two doses of measles-containing vaccine should be supplemented with measles vaccine, the interval between the two doses is ≥28 days.

Hepatitis A vaccine

Hepatitis A (hepatitis A for short) is an intestinal infectious disease mainly caused by liver damage caused by hepatitis A virus (HAV). It mainly occurs in developing countries such as Asia and Africa. My country is a high-endemic area of hepatitis A [26- 27]. The prevalence of hepatitis A is closely related to the local health status. It has obvious seasonality and often shows periodic outbreaks. The source of infection is patients in the acute phase and subclinical infections [28]. A lot of practice has proved that inoculation of hepatitis A vaccine is the most effective way to control HAV infection. As of 2007, 27 countries including China and the United States have included hepatitis A vaccine in their national immunization programs. With the application of hepatitis A defensive vaccines, the infection rate and incidence of hepatitis A in my country has shown a good trend of declining year by year [27, 29]. Hepatitis A vaccines currently include inactivated hepatitis A vaccines and live attenuated hepatitis A vaccines. My country listed the live attenuated hepatitis A vaccine as one of the expanded immunization vaccines in May 2008, and the inactivated hepatitis A vaccine belongs to category II self-funded vaccines. The vaccination procedure of the live attenuated hepatitis A vaccine in my country is one dose: 18 months of age. There are 2 doses of inactivated hepatitis A vaccine: 18 months old and 2 years old. The principle of replanting: children> 24 months of age who have not been vaccinated against hepatitis A vaccine should receive one dose of live attenuated hepatitis A vaccine. If inactivated hepatitis A vaccine is used for inoculation, two doses should be supplemented, and the interval between vaccinations is ≥6 months. If one dose of inactivated hepatitis A vaccine has been vaccinated, but the second dose of inactivated hepatitis A vaccine is unconditionally vaccinated, one dose of live attenuated hepatitis A vaccine can be used to complete the reinoculation at an interval of ≥6 months.

China's non-immunization schedule vaccines

13-valent pneumococcal vaccine

Pneumococcus is the main pathogen causing serious diseases such as pneumonia, meningitis, and bacteraemia in children. It is also a common cause of acute otitis media and sinusitis. Pneumococcal diseases (PDs) are one of the world's serious public health problems, bringing serious health threats and a heavy economic burden to children and adults around the world. The early use of vaccine prevention can effectively reduce their morbidity and mortality [30].The 13-valent pneumococcal polyglycoprotein conjugate vaccine (PCV13) is the pneumococcal conjugate vaccine with the widest serotype coverage since the 7-valent pneumococcal polyglycoprotein conjugate vaccine (PCV7), including 1, 3, 4, 5, 6A, 6B, The capsular polysaccharides of 13 serotypes such as 7F, 9V, 14, 18C, 19A, 19F and 23F can induce effective protective antibodies in infants and young children and exert a good immune effect. According to estimates by the World Health Organization (WHO), in 2008, about 476,000 children younger than 5 years old died of PDs. PDs are the world's leading cause of vaccine-preventable death for children younger than 5 years old [31], and the incidence and mortality of PDs in developing countries Much higher than that in developed countries, China ranks second in the world in the number of PDs in children under 5 years old, accounting for 12% of the total number of cases [32]. The PCV13 recommended immunization program currently approved in my country is basic immunization at 2, 4, and 6 months, and booster immunization at 12-15 months.

Hand-foot-mouth vaccine

Hand, foot and mouth disease (HFMD) is an acute infectious disease, with enterovirus infection as the main pathogen, especially EV71. In the past 20 years, HFMD has occurred frequently worldwide, especially in the Asia-Pacific region [33], and a small number of children with toxic encephalitis, brainstem encephalitis, pulmonary edema, acute flaccid paralysis and other severe illnesses or even death [34]. HFMD has become one of the important public health problems in the Asia-Pacific region. The EV-A71 vaccine developed in my country was first approved in December 2015 [35]. There are two doses of hand-foot-mouth vaccine immunization in my country: starting at 6 months of age and 7 months of age, the interval between the two doses is ≥ 28 days.

Oral live attenuated rotavirus vaccine

Rotavirus (RV) is the main cause of severe dehydrating diarrhea in children under 5 years of age worldwide. According to estimates by the World Health Organization (WHO), there are more than 25 million outpatient cases and more than 2 million hospitalized cases caused by RV infection each year [36]. The application of oral rotavirus live attenuated vaccine (ORV) will be of great significance in reducing the morbidity and mortality of RV gastroenteritis (RVGE) [37]. At present, the large-scale production and use of ORV abroad is mainly pentavalent human-bovine reassortant ORV (ORV-HB). The main production and use in my country is Lanzhou sheep ORV (ORV-L). The imported five-valent oral immunization program has three doses: 6 weeks of age at the beginning, no more than 32 weeks of age at the latest, 4 to 10 weeks between the 2 doses, and no more than 10 weeks. There are 3 doses in the domestic unit price oral round immunization program: the initial month is 6 weeks of age, and the interval between the two doses is ≥ 12 months.

Haemophilus influenzae type b

Haemophilus influenza type b is one of the main pathogens causing invasive infections such as meningitis, pneumonia, bacteraemia, epiglottitis and pericarditis. Children under 5 years old are the main targets of infection. With the large-scale application of Haemophilus influenza type b vaccine (HIB) in some developed countries and regions, the incidence of infection caused by Haemophilus influenza type b has dropped rapidly, but in countries and regions that have not introduced Hib, influenza b Infections caused by Haemophilus bacteria are still one of the serious public health problems. According to statistics from the World Health Organization (WHO), 386,000 people die from Haemophilus influenza type b infections worldwide each year, and the dead are mainly distributed in developing countries [38]. There is currently no uniform Hib immunization program in my country, and some experts recommend a basic immunization program of 2 or 3 doses for children under 5 years of age [39].

Varicella vaccine

Varicella is an eruptive disease caused by the primary infection of varicella-zoster virus (VZV). The appearance of blisters on the skin and mucous membranes of the whole body with fever in batches characterize it. It is common in children and is highly infectious. Varicella is self-limiting, but the infection of immunodeficiency patients can be complicated by pneumonia, meningoencephalitis, etc. Infection during pregnancy can lead to neonatal varicella syndrome. After the chickenpox is cured, the virus can be lurking in the posterior root ganglion of the spinal cord. When the body's resistance is reduced, the virus is activated to replicate and cause herpes zoster [40-41]. Vaccination with live attenuated varicella vaccine (varicella vaccine for short) is the most effective preventive measure. Live attenuated varicella vaccine has been used in Japan for many years. In 1995, the vaccine was approved for production in the United States and is recommended for use in children aged 1-12 years. The effect can reach 90%. Even if the infection occurs after vaccination, the clinical symptoms of the child are mild, usually no fever, and no more than 50 chickenpox rashes. There are 2 doses of varicella vaccine in my country: 1 year old and 2 years old, the interval between the two doses is ≥ 12 months.

Vaccine replenishment in non-immunization programs

Based on prioritizing vaccinations in the national immunization program, it is recommended to continue to use the same type of non-immunization program vaccine to complete subsequent doses of vaccinations for those who postpone vaccination against non-immunization programs. Vaccination is postponed due to the epidemic. If the recipient is older than the vaccination instructions, except for oral rotavirus vaccine, other vaccines can continue to complete the remaining doses after the recipient or his guardian's informed consent. If the person or his guardian disagrees, the subsequent vaccination will be cancelled.

Research Progress of Childhood Vaccines

Multivalent vaccine

More than a dozen enteroviruses cause hand, foot and mouth disease (HFMD). Enterovirus 71 (EV-A71) and Coxsackie virus A group 16 (CV-A16) alternate or co-epide in many countries around the world. Alternatively, an outbreak of hand, foot and mouth disease in the area [42-43]. After 2010, CV-A6, CV-A10 and other pathogens gradually replaced EV-A71 and CV-A16 in Asia, America and Europe as the main pathogens causing HFMD outbreaks or epidemics [44-48]. The HFMD pathogen spectrum is complex and changeable, which brings challenges to the development of HFMD vaccines. However, there is no cross-reaction between different serotypes of EV. The single-valent EV-A71 vaccine cannot prevent HFMD and related diseases caused by other pathogens. A multivalent HFMD vaccine should be developed [49]. At present, many enterprises and R&D institutions in my country have gradually carried out related research and development.

Combination vaccine

The main purpose of combining several vaccine antigens is to reduce the number of injections while preventing more diseases. However, the solubility, physical compatibility and antigen stability of each antigen component must be considered. In addition, the combination vaccine must avoid some potential problems such as antigen competition and expression inhibition. Of course, side effects cannot be aggravated. At present, the combined vaccines in my country's immunization program include DTP triple, MMR triple, DTP, leprosy, MMR and other dual vaccines. There are also many types of combined vaccines outside the immunization program. Quadruple vaccine (DTaP-Hib), five combination vaccine (DTaP-Hib-IPV) and six-combination vaccine (DTaP-Hib-IPV-HBV). In the future, the use of sexually transmitted diseases DTP or DTap as the "backbone" to add other antigens will form a 6-unit, 7-unit or even higher combined vaccine. Therefore, the future development direction of combined vaccines for children will be to enable children to obtain protection against diphtheria, tetanus, pertussis, polio, Haemophilus influenzae type b, respiratory syncytial virus, and parainfluenza viruses in the first few months of life. 1, 2, 3, pneumococcal infection (including otitis media), meningococcal infection, hepatitis A, B and C rotavirus, adenovirus and tuberculosis protection [50].

DNA vaccine

Plasmid DNA vaccine as a new way of immunization has many potential advantages over tuberculosis vaccine. Through the delivery of gene pipette tips, myoblasts, muscle cells and Langerhans, cells, absorb immune DNA. The introduced DNA will remain free for 1 year or more, and the antigen will be expressed and secreted in the cytoplasm. Through the histocompatibility complex (MHC1) pathway, humoral and cellular immune responses are induced. Its advantage is that the intracellular expression of antigen can induce cytotoxic T lymphocyte (CTL) response, and in the absence of adjuvant, it can induce humoral immunity. In addition, prolonging the expression of antigens can meet the needs of enhancing immunity. DNA technology is relatively simple, the cloning of new

antigens is very rapid, it is easy to prepare and purify, and DNA vaccines are very stable. To date, only a few veterinary DNA vaccines have been licensed, and no DNA vaccines have been approved for use in humans. Some experimental human DNA vaccines are undergoing phase I, II or III clinical trials, and their effectiveness and safety still need clinical verification [51].

Genetically engineered vaccine

Genetically engineered vaccines are the use of genetic engineering methods or molecular cloning techniques to isolate the protective antigen gene of a pathogen, and transfer it into a prokaryotic or eukaryotic system to express the protective antigen of the pathogen to make a vaccine, or to correlate the virulence of the pathogen The gene is deleted, making it a gene-deleted vaccine without virulence-related genes. For example, hepatitis B surface antigen and detoxified pertussis toxin are two commercial genetically engineered vaccines. At present, the new vaccines that have been used and are being developed using genetic engineering technology mainly include genetic engineering subunit vaccines, genetic engineering live vector vaccines, nucleic acid vaccines, synthetic peptide vaccines, genetically modified plant edible vaccines, etc. These vaccines are collectively referred to as genetic engineering vaccines. The disease factors that a large number of candidate vaccines prevent at the same time include mulberry spirochetes, herpes simplex virus, influenza virus, human immunodeficiency virus, Plasmodium falciparum and Helicobacter pylori, etc. and clinical trials are ongoing. The ideal antigens for the transfer vector for expression include viruses (poxvirus, adenovirus, influenza virus) and bacteria (Salmonella, Shigella, and BCG). Genetic engineering vaccine technology is a new and promising biotechnology, which has many advantages that traditional vaccines cannot match [52].

Conclusion

Vaccination is recognized by the international community as the most economical, simplest and most effective measure to prevent and control diseases. This year marks the 42nd anniversary of the implementation of my country's immunization planning policy. With the joint efforts of past generations of immunization planning workers, my country's immunization planning cause has made brilliant achievements. In 2000, polio was eliminated, and the incidence of infectious diseases such as hepatitis B and measles that seriously affected children's health was greatly reduced. In the past few decades, my country has made major achievements in vaccine development and production. With the continuous improvement of living standards, the public's demand for non-immunization program vaccines is also increasing. As a supplement to the first type of vaccine, non-immunization program vaccines also play a protective role in the health of the people [53]. In the future, the country should pay more attention to vaccine research and development and innovation, and at the same time strengthen the supervision of the vaccine market to protect the health of the people and national security. Looking back on the past, we are proud of our achievements, and looking forward to the future, we will not forget our original aspirations and move forward under the guidance of the "Healthy China" strategy, and continue to strive to protect the health of the people!

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