Vaccination and Children's Health

2024 Version

Written and edited by: The Review Committee for Vaccination Guidelines
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Introduction

Children are often ill and sometimes become extremely sick; vaccination can protect them from several serious illnesses.

This brochure has been created to provide you with information about vaccination and to allow you to have your child vaccinated safely.

We hope that this brochure will enhance the health and growth of your child.

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The 2024 edition is based on revisions as of February 2024.

You can receive the latest information from your municipality (including special wards; the same applies below). This information is also available from the websites of the

Ministry of Health, Labour and Welfare (https://www.mhlw.go.jp/english/) and the

Infectious Disease Surveillance Center, National Institute of Infectious Diseases (https://www.niid.go.jp/niid/en/).

In the event of amendments to laws or regulations, the Notice of Revision, etc. will be uploaded to our website (https://www.yoboseshu-rc.com).

1. Get your child vaccinated!

The immunity to diseases which mothers give their infants almost completely disappears 3 months after birth for pertussis and 12 months after birth for measles. Consequently, after these periods, infants must ward off disease by producing their own immunity. Vaccination supports this defense.

Children go outside more often and interact with more people as they grow; consequently, they are at higher risk of infection. We recommend that you learn about vaccination and have your child vaccinated for his/her health.

● Infections

Infections are caused by pathogens, including viruses and bacteria, which invade the body and multiply. Symptoms may include fever, cough, and headache, depending on the type of pathogen.

2. What is vaccination?

Vaccination is the administration of attenuated forms of viruses and bacteria or of their toxins which cause infectious diseases such as measles and pertussis. Giving these attenuated forms produces immunity against these diseases. A “vaccine” is a preparation used for vaccination.

Vaccines cannot be prepared for all infectious diseases. Due to their nature, vaccines cannot be produced for some viruses and bacteria.

3. Vaccination validity

Vaccination is performed to prevent a target disease or reduce its severity in the event it is contracted; however, immunity is not established in some children because of their characteristics and physical condition. If there is a desire to confirm whether immunity has been established, there are blood tests which measure the levels of antibodies in the blood.

In addition, with some vaccines, immunity gradually diminishes even after it has been established, and such vaccines require boosters at specific intervals to maintain long term immunity. (See 5. (3) Vaccine types and characteristics on page 4)

4. Routine vaccination and voluntary vaccination

Vaccination includes routine vaccination and voluntary vaccination. With regard to routine vaccination, the Preventive Vaccination Law defines the target diseases, subjects and vaccination schedules.

Vaccination is carried out during periods appropriate to each disease. Please refer to "List of recommended periods for routine vaccination (Category A disease)" on page 8 for recommended vaccination periods (standard vaccination periods).

Routine vaccination

Routine vaccinations are the vaccinations stipulated by the "Preventive Vaccination Law" and are divided into vaccinations for Category A and Category B diseases. As a general rule, the cost is paid by the local governments for those subject to vaccination against Category A diseases, so they can be vaccinated at public expense. Vaccination against Category B diseases may be partly covered by public expense. From January 30, 2013, special measures have been set for children who were unable to receive routine vaccination due to a long-term serious illness. For details, please check the information of your health center/municipal office.

Category A disease	The main focus is on mass prevention and prevention of serious illnesses. The person (guardian) is obliged to make an effort and is recommended to be vaccinated by the government.
・Rotavirus infection ・Hepatitis B ・Hib infection ・Pneumococcal infection in children ・Diphtheria ・Pertussis ・Tetanus ・Polio (Acute poliomyelitis) ・Tuberculosis (BCG) ・Measles・Rubella・Varicella・Japanese encephalitis・Human papillomavirus (HPV) infection	

Category B disease	The main focus is on personal prevention. The person (guardian) is not obliged to make an effort and is not recommended to be vaccinated by the government.
・Seasonal influenza infection* ・Pneumococcal infection in elderly ・COVID-19 infection in the elderly	

*Vaccination against seasonal influenza for children is voluntary.

Voluntary vaccination

Voluntary vaccinations are vaccinations other than the "routine vaccinations" stipulated in the "Preventive Vaccination Law". As a general rule, the cost required for vaccinations is borne by the individual. Some local governments pay part or all of the cost depending on the need for vaccination. Please check the information of your health center/municipal office.

5. Let's make a vaccination plan for your child

(1) Notice of vaccination

Routine vaccination is carried out by the municipal office in accordance with the Preventive Vaccination Law. A notice of vaccination is usually sent to parents/guardians individually. Since the notice is sent on the basis of the Basic Resident Register and the Residence Card, make sure to report when a baby is born or when you move.

(2) Set a rough schedule for vaccination

Routine vaccinations are, in principle, given individually. Determine a specific schedule and order for vaccinations after considering municipal programs, the physical condition your child, and the state of disease provenance, and consulting with your family doctor.

Note that some municipalities may offer mass vaccination (performed on specified dates at specified sites such as health centers) of the BCG vaccine.

(3) Vaccine types and characteristics

Vaccines used for immunization are as follows: live vaccine; inactivated vaccine; and for COVID-19, mRNA vaccine.

Live vaccine

Live vaccines are made of attenuated live bacteria and viruses (live bacteria and viruses whose pathogenicity has been weakened). Resistance (immunity) to the disease is established similarly to actually being infected by it. After vaccination, attenuated bacteria and viruses (bacteria and viruses whose pathogenicity has been weakened) start multiplying; consequently, vaccines can cause mild symptoms, including fever and rash, depending on

the vaccine. It takes about one month to establish sufficient resistance (immunity). However, some vaccines require boosters because their resistance (immunity) may gradually decline and weaken.

Types of live vaccines	・Rotavirus vaccine ・BCG vaccine ・Measles-rubella (MR) vaccine ・Measles vaccine ・Rubella vaccine ・Varicella (chicken pox) vaccine ・Mumps vaccine ・Yellow fever vaccine ・Intranasal influenza vaccine

Inactivated vaccine

Inactivated vaccines are made by killing the virus or bacteria, extracting the components required to develop resistance (immunity) and eliminating their virulence (pathogenicity). The bacteria and viruses do not multiply, and several shots are required to establish resistance (immunity). Two or three vaccine shots are given at certain intervals to establish a basic resistance (immunity), after which a booster is given several months to one year later to enhance resistance (immunity) to a sufficient level. However, the resistance (immunity) declines gradually. To keep the resistance (immunity) for a long time, a booster is required at certain intervals, depending on the characteristics of the vaccine.

Types of inactivated vaccines	・Hepatitis B vaccine ・Hib vaccine ・Pediatric pneumococcal vaccine ・Diphtheria-pertussis-tetanus and inactivated polio vaccine (DPT-IPV) ・Quintuple vaccine (DPT-IPV-Hib) ・Diphtheria-pertussis-tetanus vaccine (DPT) ・Diphtheria-tetanus vaccine (DT) ・Inactivated poliovirus vaccine (IPV) ・Japanese encephalitis vaccine ・Human papillomavirus vaccine ・Seasonal influenza vaccine ・Meningococcal vaccine ・Hepatitis A vaccine ・Rabies vaccine ・Tetanus vaccine (T)

mRNA vaccine

COVID-19 vaccines include vaccines which are manufactured differently from conventional methods, namely mRNA vaccines (vaccines in which mRNA, or messenger RNA, the blueprint of the antigen protein on the surface of the COVID-19 virus, is encased in lipid nanoparticles), and recombinant viral vector vaccines, in which the COVID-19 spike protein gene is inserted into non-replicating adenovirus. Since these vaccines cannot be classified into the conventional categories of live and inactivated vaccines, they constitute a separate category. Inactivated COVID-19 vaccines are also in practical use. Live vaccines are also being developed.

Types of mRNA vaccines	・COVID-19 vaccine

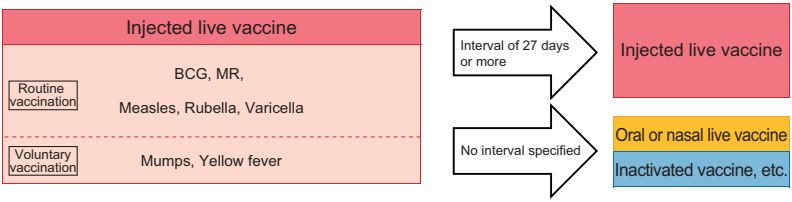
(4) Intervals at which different vaccines are given

On October 1, 2020, the vaccination intervals when receiving different vaccines were revised.

Vaccines used for immunization include live, inactivated, and mRNA vaccines. When injecting a live vaccine, it is necessary to observe a certain interval between injections.

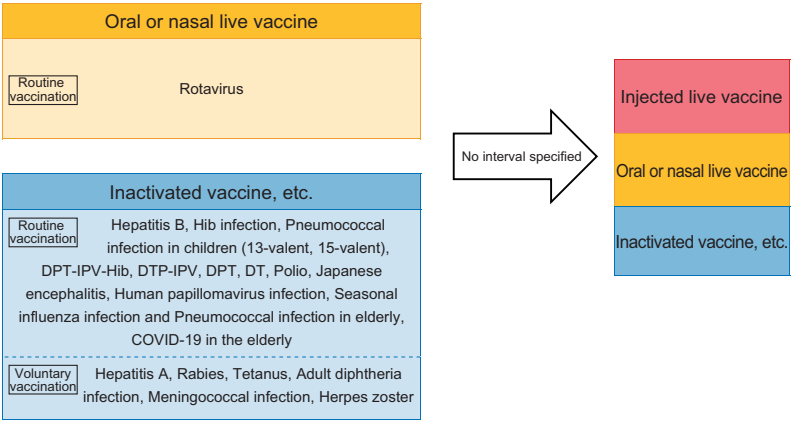
In certain cases, more than one kind of vaccine may be received at the same time. Consult with your doctor thoroughly.

If your child is to be vaccinated several times with the same vaccine, please make sure that the specified intervals are adhered to.



*The interval from the day after vaccination with an injected live vaccine to the day of another injected live vaccine shall be 27 days or more.

*The interval from the day after vaccination with an injected live vaccine to the day of vaccination with a live oral vaccine or inactivated vaccine is not specified.



(Caution)

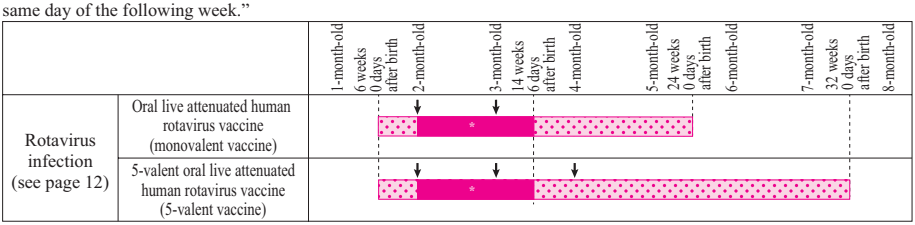
- Symptoms such as fever and swelling at the injection site may occur over a period of several days after vaccination. Regardless of whether it is within the period in which additional vaccination is allowed, only proceed with vaccination after verifying that there are no physical health issues, such as fever or swelling at the injection site.
- Different vaccinations may be given at the same time when specially approved by a doctor.
- For vaccines which require multiple inoculations, please follow the provisions outlined in package inserts, etc., regarding vaccination intervals.

*COVID-19 vaccination of the elderly will be conducted on a routine basis after COVID-19 is designated as Category B disease in FY2024.

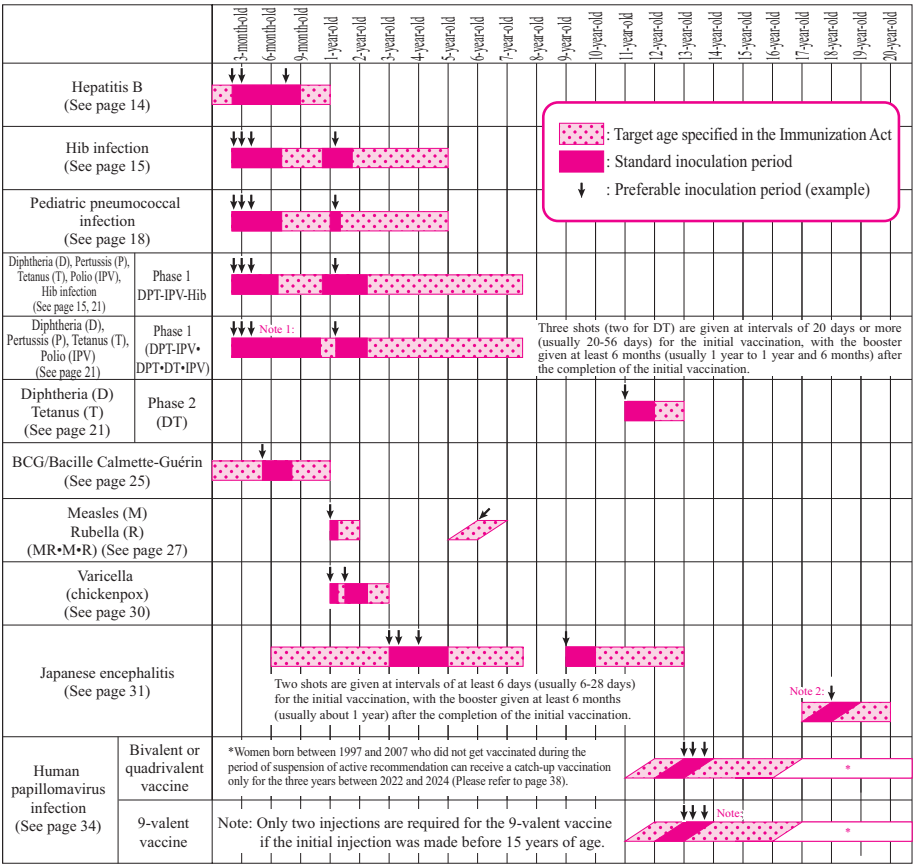
At the 55th Meeting of the Subcommittee on Vaccination and Vaccines of the Health Sciences Council in February 2024, approval was given for the simultaneous injection of COVID-19 vaccine and other vaccines without an interval requirement when deemed necessary by a physician. These measures are similar to those for other vaccines except injectable live vaccines.

List of recommended periods for routine vaccination (Category A disease)

[Note] The starting date for calculating the vaccination interval is the day following the day of vaccination. The length of vaccination intervals are established in laws and ordinances. For example, "an interval of one week" means "on or after the same day of the following week."



*The standard vaccination period for the initial vaccination is between 2 months after birth and 14 weeks 6 days after birth.



Note 1: If DT is used for phase 1, it is to be given no earlier than 3 months after birth.

Note 2: Persons born between April 2, 1995 and April 1, 2007 who were unable to receive the phase 1 and 2 vaccine are able to receive the vaccine as a routine vaccination if under the age of 20.

6. Before having your child vaccinated

Please confirm the following before vaccination

1 Is your child in good health?
2 Do you understand the necessity for vaccination and the benefits and possible risks (adverse reactions) of the vaccine that will be given to your child today?
If you have any questions, please write them down.
3 Did you bring your maternal and child health handbook with you?
4 Did you complete a vaccination screening questionnaire?

(1) General precautions

Vaccination should be performed when your child is in good health. Always take note of the physical condition and characteristics of your child. If you have any concerns, do not hesitate to consult your family doctor, healthcare center, or the municipal office in charge, in advance.

To have your child vaccinated safely, we recommend that you make the decision whether to receive the vaccination on the appointed day after taking the following into consideration:

a) Observe your child carefully from the morning on the day of vaccination, and confirm that he/she is well.
Even if vaccination is scheduled, if your child appears sick, consult your family doctor and decide whether your child should be vaccinated or not.
b) Thoroughly read the information about vaccination provided by the municipal office so that you fully understand the necessity and possible adverse effects of the vaccines.
If you have any questions, ask the doctor who is to vaccinate your child before vaccination.
c) Make sure to bring your maternal and child health handbook.
d) The screening questionnaire contains important information for the doctor in charge of vaccination. Please fill in the form completely and accurately.
e) We recommend that the child being vaccinated be accompanied by a parent/guardian who is familiar with the child's usual physical condition.

A child can only be vaccinated if a parent/guardian fully understands the benefits of and possible adverse reactions to vaccination and agrees to have the child vaccinated.

(2) The following persons cannot receive vaccination:

a) A child with an obvious fever (37.5℃ or higher)

The vaccinating doctor and guardian (patient) are to thoroughly check the health condition of persons presenting with a body temperature slightly higher than 37.5℃ due to such reasons as a high baseline body temperature, and make judgments accordingly as to whether to perform the vaccination.

b) A child with a severe acute illness

As a general rule, children with acute, severe illnesses should not be vaccinated on that day, as the course of such illness can be unpredictable.

c) A child who has had anaphylaxis to any component of the vaccine preparation to be given on that day

"Anaphylaxis" is an acute, severe systemic allergic reaction, usually within 30 minutes after vaccination, including excessive sweating, a swollen face, systemic severe urticaria, nausea, vomiting, hoarseness, and respiratory distress, resulting in shock.

d) Women eligible for the measles, rubella, varicella (chickenpox), and mumps vaccination and are known to be pregnant

This is a regulation not directly concerning children but important for persons who will receive voluntary vaccination.

e) As concerns the BCG vaccination (hereinafter referred to BCG), a child with a predisposition to keloids

f) Persons who are eligible for the hepatitis B vaccination and who have received the hepatitis B vaccine after birth as part of the mother-to-infant transmission prevention program

g) Children eligible for rotavirus vaccination who have a clear history of intussusception, who have a congenital abnormality of the gastrointestinal tract (except for children who have completed treatment for said abnormality), or who have been found to have a severe combined immunodeficiency disease

h) Other conditions that a doctor considers inappropriate

Even if your child does not meet the above criteria a) to f), he/she cannot be vaccinated if a doctor decides that doing so would be inappropriate.

(3) Children who require careful consideration in receiving a vaccination

Parents/guardians to whom the following may apply should have their child seen by their family doctor in advance to determine whether the child can be vaccinated. If vaccination is to take place, it should be performed by the family doctor, or at another medical institution provided a note or letter, etc. can be obtained from the family doctor.

a) A child who is being treated for a heart, kidney, liver, or blood disease, or a developmental disorder.

b) A child who has had a fever within 2 days of a previous vaccination or an allergic reaction, including rash and urticaria.

c) A child who has had a seizure in the past.
The decision of whether a child should be vaccinated depends on the age at which the seizure occurred, the presence or absence of fever, subsequent seizures, and the type of vaccine. Please consult the child's doctor before vaccination.

d) A child who has been diagnosed with immunodeficiency in the past or has a family member or relative with immunodeficiency (for example, a person who repeatedly had perianal abscesses as a baby).

e) A child who is allergic to the vaccine's components, such as eggs, antibacterial agents, and the stabilizers used in any step of vaccine production.

f) In the case of BCF vaccination, a child who is suspected to have been infected with tuberculosis in the past, such as having had extended contact with a tuberculosis patient in the family.

g) In the case of rotavirus vaccination, a child with an active gastrointestinal illness or gastrointestinal disorder such as diarrhea.

(4) General precautions after receiving vaccination

a) For 30 minutes after the vaccination, observe your child at the medical institution (facility) or ensure that a doctor can be contacted immediately. Acute adverse events often develop during that time.

b) Watch for possible adverse reactions for up to 4 weeks (for live vaccines) or 1 week (for inactivated vaccines) after vaccination.

c) Keep the vaccination site clean. Bathing is allowed, but avoid rubbing the vaccination site.

d) Avoid strenuous physical activity on the day of vaccination.

e) If a child experiences an abnormal reaction at the vaccination site or has a change in physical condition after vaccination, consult a doctor immediately.

7. Diseases preventable by vaccination and vaccines

Each child has a unique physiological makeup. In rare cases, varying degrees of adverse reactions may occur. It is important for you to decide whether to have your child vaccinated after detailed consultation with your doctor, who understands the physical status of your child.

◆ Rotavirus infection

(1) Cause and course

Rotavirus is a cause of acute gastroenteritis seen around the world and often seen primarily in infants and children under the age of 5 years old. Primary symptoms include diarrhea, vomiting, and fever and may also occasionally be accompanied by dehydration, spasms, liver dysfunction, and renal failure, and, rarely, acute encephalopathy. It can infect and cause illness any number of times, regardless of age, but first-time infection during infancy causes the most serious illness, with repeated infection thereafter resulting in more and more mild illness.

(2) Rotavirus vaccines (live vaccines)

There are two rotavirus vaccines – the oral live attenuated human rotavirus vaccine (Rotarix®; hereafter referred to as the monovalent vaccine), which uses attenuated rotavirus; and the 5-valent oral live attenuated human rotavirus vaccine (RotaTeq®; hereafter referred to as the 5-valent vaccine), which uses reassortant rotavirus. Both vaccines provide about 80% protection from gastroenteritis caused by rotavirus infection, and about 95% protection from serious rotavirus infection.

Rotavirus can infect and cause illness any number of times, regardless of age, but first-time infection during infancy causes the most serious illness, with repeated infection thereafter resulting in more and more mild illness. Accordingly, with the primary aim of preventing such first-time infection, vaccination is administered in early infancy.

With the first rotavirus vaccine introduced in the United States, it was found that intussusception, a serious illness in infants and young children, frequently occurred as an adverse reaction, and sales of this product were halted. Both of the two varieties of rotavirus vaccine in use around the world today have been confirmed to have a lower risk of intussusception than the first rotavirus vaccine introduced in the United States via large-scale clinical trials.

The risk of intussusception is increased during the week after receiving the first rotavirus inoculation.

In comparing the risks (the occurrence of adverse reactions such as intussusception) and

benefits (prevention of serious rotavirus infection) of rotavirus vaccination, it is believed that preventing rotavirus infection is more beneficial to children, and more and more countries around the world are introducing the rotavirus vaccines.

If you notice even one of the following in your child after rotavirus vaccination, consider the possibility of intussusception and consult with a doctor immediately: periodic dysphoria, abdominal pain, repeated vomiting, intense crying, or bloody stool.

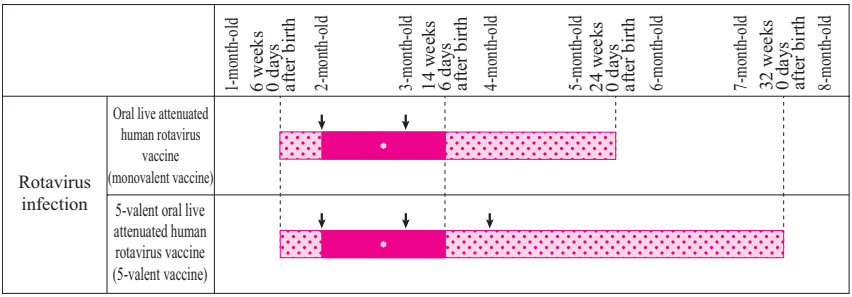
Rotavirus was made a routine vaccination on October 1, 2020.

Eligibility for the routine vaccination is children born on or after August 1, 2020.

The inoculation ages and number of inoculations differ according to the type of vaccine used. The monovalent vaccine (Rotarix®) is given in 2 inoculations separated by an interval of 27 days or more for children between 6 weeks 0 days after birth and 24 weeks 0 days after birth. The 5-valent vaccine (RotaTeq®) is given in 3 inoculations separated by intervals of 27 days or more for children between 6 weeks 0 days after birth and 32 weeks 0 days after birth. Note that in order to avoid the period in which there is a high incidence of intussusception, it is considered desirable to complete the initial inoculation by 14 weeks 6 days after birth.

The incidence of severe cases (cases deemed to be serious by the reporter) among suspected cases of adverse reactions (adverse events) reported by medical institutions was 0.003% for the monovalent vaccine (Rotarix®) and 0.0021% for the 5-valent vaccine (RotaTeq®). (The incidence reported from April 1, 2013 to September 30, 2023. Source: January 2024 documents 2-23 and 2-24 from the 100th Working Group Meeting on Adverse Events, the Subcommittee on Vaccination and Vaccines of the Health Sciences Council.)

(3) Vaccination schedule



*The standard vaccination period for the initial vaccination is between 2 months after birth and 14 weeks 6 days after birth.

◆ Hepatitis B

Since October 2016, the hepatitis B vaccine has been given as a routine vaccination to all children born on or after April 1, 2016. The cost of vaccinations to newborns of hepatitis B-positive (HBs antigen positive) mothers will continue to be covered by health insurance, and in the case of accidental exposure to hepatitis B positive blood etc., the cost of the inoculation will continue to be covered by workers' compensation or health insurance.

(1) Cause and course

When a person is infected by the hepatitis B (HB) virus, he or she may develop acute hepatitis and recover, or progress to chronic hepatitis. In some cases, fulminant hepatitis may occur with severe symptoms which may result in death. In other cases, the virus may hide in the liver without causing any obvious symptoms, and develop into chronic hepatitis, cirrhosis, or hepatic cancer after a period of years. It is known that the younger the patient, the less clear the symptoms of acute hepatitis and the more likely the virus will hide, resulting in persistent infection. Infections occur through mother-infant transmission from an HB virus positive (HBs antigen positive) mother to her newborn, through direct contact with HB positive blood or bodily fluids, or through sexual contact with an individual who is HB positive.

(2) Hepatitis B vaccine (inactivated vaccine)

Vaccination with the hepatitis B (HB) vaccine, especially in children, is aimed primarily at preventing persistent infection by the virus and the future potential occurrence of chronic hepatitis, cirrhosis, or hepatic cancer, rather than at preventing hepatitis in the short term.

Previously, newborn infants of HB virus positive mothers were given the hepatitis B vaccine plus hepatitis B immunoglobulin as soon as possible after birth to prevent mother-to-child

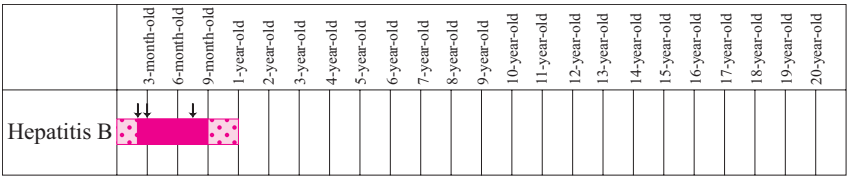
transmission. Now, however, in order to have more people receive the hepatitis B vaccine and reduce the number of future sufferers of chronic hepatitis, cirrhosis, and hepatic cancer, routine vaccination began in October 2016 for all children born on or after April 1, 2016, in addition to the mother-to-child transmission prevention program.

Note that the mother-to-child transmission prevention program will continue to be covered by health insurance.

Children eligible for routine HB vaccination are those born on or after April 1, 2016 and under 1 year of age. The standard schedule is between the time the child turns 2 months and up to 9 months, in which two subcutaneous injections are given with an interval of at least 27 days between the first and second injections, and another subcutaneous injection given after an interval of at least 139 days after the first injection.

Adverse reactions to the HB vaccine have been reported in about 10% of people who received the vaccine to date, and include lethargy, headache, and swelling/redness/pain at the vaccination site, etc. However, the vaccine is being given to newborns and infants without problems. The incidence of severe cases (cases deemed to be serious by the reporter) among suspected cases of adverse reactions (adverse events) reported by medical institutions was 0.0008%. (The incidence reported from April 1, 2013 to September 30, 2023. Source: January 2024 document 2-22 from the 100th Working Group Meeting on Adverse Events, the Subcommittee on Vaccination and Vaccines of the Health Sciences Council.)

(3) Vaccination schedule



◆ Hib infection

(1) Cause and course

Haemophilus influenzae, especially Haemophilus influenzae type b, is a problematic pathogen for infants and small children, causing not only superficial infections such as otitis media, sinusitis, and bronchitis, but also deep (systemic) infections (also called invasive infections) such as meningitis, sepsis, and pneumonia. Prior to 2010, the incidence of meningitis caused by Hib was 7.1-8.3 out of a population of 100,000 aged less than 5 years. It was estimated

that about 400 become infected with meningitis per year and about 11% of those experience poor outcomes*. Children aged 4 months or more and less than 1 year accounted for a half of total patients. (*Cited from material provided by the Vaccination Working Group, Section of Infectious Diseases, Health Science Council of MHLW.) Now that the Hib vaccine is widely used, invasive Hib disease is nearly unseen.

(2) Freeze-dried Haemophilus b conjugate vaccine (Hib vaccine) (inactivated vaccine)

In April 2024, the quintuple vaccine (DPT-IPV-Hib) was made a routine vaccination to be used for the prevention of Hib infection as a general rule.

In the quintuple vaccine, the Hib vaccine is added to the quadruple vaccine (DPT-IPV). It is considered to have the same level of safety as the existing quadruple and Hib vaccines. It can be delivered subcutaneously or intramuscularly. For number and interval of inoculations see Page 8.

Note that the Hib vaccine can also be used for the time being.

This section discusses the Hib vaccine. For the latest information relating to routine vaccination of the quintuple vaccine, please refer to information and Implementation Guidelines for Routine Immunization issued by the Ministry of Health, Labour and Welfare.

Haemophilus influenzae is classified into 7 categories, with type b being the main cause of serious disease; consequently, type b is used for vaccination. This vaccine is used extensively throughout the world, and was authorized for use in Japan in December 2008 and made a routine vaccination in April 2013.

This vaccine may be given simultaneously with other vaccines when the physician determines it to be necessary and the child's guardian gives consent. Each vaccine can also be given separately.

In Europe and the United States, invasive Hib infections decreased dramatically after the vaccine was introduced. Reduction has been similarly dramatic in Japan after introduction of routine vaccination, and Hib infections are now nearly unseen. The World Health Organization (WHO) highly recommended routine Hib vaccinations for infants and children in 1998; consequently, Hib vaccination has been introduced in more than 110 nations and its efficacy has been evaluated highly.

Adverse reactions (at the time of approval) are mainly local reactions including redness (44.2%), swelling (puffiness) (18.7%), induration (lump) (17.8%), and pain (5.6%); as well

as systemic reactions including fever (2.5%), dysphoria (14.7%), and loss of appetite (8.7%). (See package insert [3rd ver.] revised in August 2023)

The incidence of severe cases (cases deemed to be serious by the reporter) among suspected cases of adverse reactions (adverse events) reported by medical institutions was 0.0019%. (The incidence reported from April 1, 2013 to September 30, 2023. Source: January 2024 document 2-19 from the 100th Working Group Meeting on Adverse Events, the Subcommittee on Vaccination and Vaccines of the Health Sciences Council.)

Vaccination against Hib infection is conducted per the following procedures by age in months at the time of initiating the initial vaccination. The standard vaccination procedure is as described in (a) below:

a) A child aged 2 to 7 months (not exceeding the first day of 7 months) at the time of initiating the initial vaccination

The initial vaccination is conducted using a Hib vaccine provided three times at intervals of 27 days or more (20 days if required by a physician), with the standard interval being 27 (20 if required by a physician) to 56 days. The booster is conducted once at an interval of 7 months or more (usually 7 to 13 months) after the initial vaccination. It should be noted that the second and third injections of the initial vaccination are to be given by the time the child is 12 months of age, and are not to be given if the child exceeds 12 months. One booster may be given after an interval of at least 27 days (20 days if required by a physician) after the last vaccination of phase 1.

b) A child aged 7 months (the second day of 7 months) to 12 months (not exceeding the first day of 13 months) at the initiation of the initial vaccination

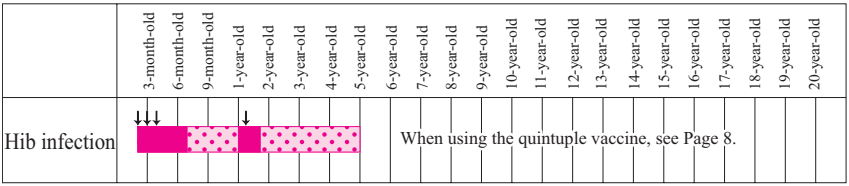
The initial vaccination is conducted using a Hib vaccine provided twice at intervals of 27 days or more (20 days if required by a physician), with the standard interval being 27 (20 if required by a physician) to 56 days. The booster is conducted once at an interval of 7 months or more (usually 7 to 13 months) after the initial vaccination. It should be noted that the second injection of the initial vaccination is to be given by the time the child is 12 months of age, and is not to be given if the child exceeds 12 months. One booster may be given after an interval of at least 27 days (20 days if required by a physician) after the last vaccination of phase 1.

c) A child aged 12 months (the second day of 12 months) to 60 months (not exceeding the first day of 60 months) at the initiation of the initial vaccination.

The vaccination is conducted using a Hib vaccine provided once.

A child who could not be vaccinated due to disease requiring long-term care is also vaccinated in this manner.

(3) Vaccination schedule



◆ Pneumococcal infection in children

(1) Cause and course

Streptococcus pneumoniae is one of two major causes of bacterial pediatric infections. This is a bacterium carried deep in the noses of many children and occasionally causes bacterial meningitis, bacteremia, pneumonia, sinusitis, and otitis media.

Prior to the introduction of the vaccine, the prevalence of bacterial meningitis caused by Streptococcus pneumoniae was 2.6-2.9 out of a population of 100,000 aged less than 5 years. It was estimated that about 150 experience meningitis per year*. Case fatality rate and frequency of secondary complications (e.g. hydrocephalus, deafness, mental disabilities) are higher than that of Hib-induced meningitis, with about 21% experiencing a poor prognosis. (*Cited from material provided by the Vaccination Working Group, Section of Infectious Diseases, Health Science Council of MHLW.) Now that the pneumococcal conjugate vaccine is in wide use, invasive infections such as pneumococcal meningitis have decreased dramatically.

(2) Adsorbed 13-valent pneumococcal conjugate vaccine

(13-valent pneumococcal conjugate vaccine) (inactivated vaccine)

In April 2024, the 15-valent pneumococcal vaccine (PCV15) was made a routine vaccination. Routine pediatric pneumococcal vaccination programs are to use the 15-valent vaccine as a general rule.

The 15-valent pneumococcal vaccine (PCV15) aims to protect against serotypes 22F and 33F in addition to the serotypes within the scope of 13-valent vaccine (PCV13). It is expected to be more effective than the current PCV13 and equally as safe. It can be delivered subcutaneously or intramuscularly. For number and interval of inoculations see Page 8.

Note that the 13-valent vaccine can also be used for the time being.

This section discusses the 13-valent vaccine. For the latest information relating to routine vaccination of the 15-valent vaccine, please refer to information and Implementation Guidelines for Routine Immunization issued by the Ministry of Health, Labour and Welfare.

The pediatric pneumococcal conjugate vaccine (13-valent pneumococcal conjugate vaccine) was developed to prevent bacterial meningitis in children, including 13 serotypes causing serious conditions in children.

This vaccine was first used in the United States as a 7-valent vaccine in 2000, and switched to a 13-valent vaccine in 2010, which is currently used as the standard vaccine in over 100 countries. It has been reported in many countries that inoculation with this vaccine reduces bacterial meningitis and bacteremia. In Japan, the vaccine was authorized for use in November 2013, and the incidence of invasive pneumococcal disease has decreased similarly.

This vaccine may be given simultaneously with other vaccines when the physician determines it to be necessary and the child's guardian gives consent. Each vaccine can also be given separately.

Adverse reactions include local reactions such as erythema (67.8-74.4%) and swelling (47.2-57.1%), and systemic reactions including fever of over 37.5˚C (32.9-50.7%). (See package insert [3rd ver.] revised in September 2021.)

The incidence of severe cases (cases deemed to be serious by the reporter) among suspected cases of adverse reactions (adverse events) reported by medical institutions was 0.0019%. (The incidence reported from October, 2013 to September 30, 2023. Source: January 2024 document 2-17 from the 100th Working Group Meeting on Adverse Events, the Subcommittee on Vaccination and Vaccines of the Health Sciences Council.)

Vaccination against pediatric pneumococcal infection is provided per the following procedures by age in months at of the time of initiating the initial vaccination. The standard vaccination procedure is as described in (a) below:

a) A child aged 2 to 7 months (not exceeding the first day of 7 months) at the time of initiating the initial vaccination.

   The initial vaccination is conducted using a 13-valent pneumococcal conjugate vaccine provided three times at intervals of at least 27 days usually by the time the child is 12 months of age. The booster is conducted once at an interval of at least 60 days after the initial vaccination, given no earlier than one day after the child turns 12 months (the standard vaccination period is between 12-15 months after birth). However, the second and third injections of the initial vaccination are to be given by the time the child is 24 months of age, and are not to be given if the child exceeds 24 months (the booster is allowed after this time). The second injection of the initial vaccination is to be given by the time the child is 12 months of age, and is not to be given if the child exceeds 12 months (the booster is allowed after this time).

b) A child aged 7 (the second day of 7 months) to 12 months (not exceeding the first day of 12

months) at the time of initiating the initial vaccination.

The initial vaccination is conducted using a 13-valent pneumococcal conjugate vaccine provided twice at intervals of at least 27 days usually by the time the child is 12 months of age. The booster is conducted once at an interval of at least 60 days after the initial vaccination 12 months after birth. However, the second injection of the initial vaccination is to be given by the time the child is 24 months of age, and is not to be given if the child exceeds 24 months (the booster is allowed after this time).

c) A child aged 12 (the second day of 12 months) to 24 months (not exceeding the first day of 24 months) at the initiation of the initial vaccination.

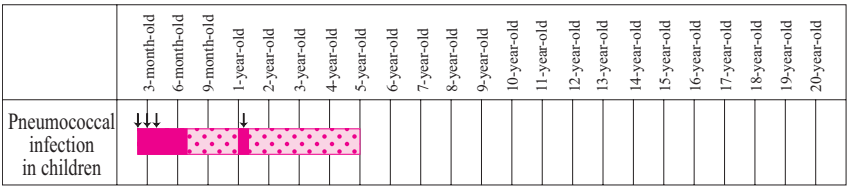
The vaccination is conducted using a 13-valent pneumococcal conjugate vaccine provided twice at intervals of at least 60 days.

d) A child aged 24 (the second day of 24 months) to 60 months (not exceeding the first day of 60 months) at the initiation of the initial vaccination.

The vaccination is conducted using a 13-valent pneumococcal conjugate vaccine provided once.

A child who could not be vaccinated due to disease requiring long-term care can also be vaccinated in this manner.

(3) Vaccination schedule



◆ Diphtheria, pertussis, tetanus, and polio (acute poliomyelitis)

In April 2024, the quintuple vaccine (DPT-IPV-Hib) was made a routine vaccination. Routine vaccination programs for diphtheria, pertussis, tetanus, and polio are to use the 5-valent vaccine as a general rule. In the quintuple vaccine, the Hib vaccine is added to the quadruple vaccine (DPT-IPV). It is considered to have the same level of safety as the existing quadruple and Hib vaccines. It can be delivered subcutaneously or intramuscularly. For number and interval of inoculations see Page 8.

Note that the quadruple vaccine can also be used for the time being.

This section discusses diphtheria, pertussis, tetanus, and polio (acute poliomyelitis). (For Hib infection see Page 15.) For the latest information relating to routine vaccination of the quintuple vaccine including Hib, please refer to information and Implementation Guidelines for Routine Immunization issued by the Ministry of Health, Labour and Welfare.

(1) Cause and course

(1) Diphtheria

Diphtheria is caused by Corynebacterium diphtheriae and is spread by droplet infection.

The improved diphtheria-pertussis-tetanus vaccine (DPT) (acellular) was introduced to the market in 1981. Today, the annual incidence of diphtheria in Japan has been zero (0) for many consecutive years, but in the Asian region, epidemic outbreaks have been seen.

The bacterium infects mainly the throat but also the nasal cavity. Even when infection occurs, diphtheria causes symptoms in only about 10% of people, while the rest of those infected become asymptomatic carriers who can transmit the disease to other people. Symptoms include high fever, sore throat, a barking cough, and vomiting; a false membrane may also form in the throat which can cause asphyxia. Patients must be monitored carefully because the bacterium produces a toxin that can cause a serious myocardial disorder or paralysis two to three weeks after the development of symptoms.

(2) Pertussis

Pertussis is caused by Bordetella pertussis and is spread by droplet infection.

Since pertussis vaccination was begun in 1950, the number of patients has decreased, but in recent years, there have been cases of pertussis in children ranging from school age to adolescence as well as in adults characterized by persistent coughing. Such people are potential sources of infection to small children, and require caution since the disease can become serious, especially in newborns and infants.

Prototypical pertussis begins with symptoms mimicking a common cold. The child then begins to cough violently and repeatedly, with a flushed face. After coughing, the patient is forced to inhale rapidly, creating a whooping sound similar to a whistle. Usually, fever does not develop. Infants sometimes present with blue lips (cyanosis), seizures (fits) or suddenly stop breathing because they are unable to breathe due to coughing. Severe complications such as pneumonia or encephalopathy are likely to develop, and these diseases may lead to death in newborns or infants.

● Droplet infection

Droplet infection is the transmission of viruses and bacteria through coughing, sneezing, conversation, etc. Viruses and bacteria enveloped in sprays of saliva and airway secretions are spread through the air to people within one meter.

(3) Tetanus

Clostridium tetani does not spread from person to person. The bacteria are usually found in soil and enter the body through wounds in the skin. The bacteria multiply in the body and produce a toxin, causing tonic muscle spasms. Half of all patients are infected through a small skin wound not noticed by themselves or the people around them. As the bacteria are found in soil, opportunities for infection are constant. If a pregnant mother has immunity, the newborn is protected from tetanus during delivery.

(4) Polio (acute poliomyelitis)

Polio (acute poliomyelitis) is also known as "infantile paralysis." Pandemics occurred repeatedly in Japan until the early 1960s. Owing to vaccination, the last occurrence of a patient paralyzed by a wild strain of the polio virus was in 1980. The WHO declared the eradication of poliomyelitis from the Western Pacific Region including Japan in 2000. At present, there are only two polio-endemic countries, Pakistan and Afghanistan, and global polio eradication seems no longer a dream, but the world remains vigilant against polioviruses.

The polio virus infects through the mouth and proliferates in the cells of the pharynx and small intestine. The polio virus is said to multiply for 4 to 35 days (mean: 7-14 days) in the cells of the small intestine. Viruses thus multiplied are excreted in feces and taken through the mouth of a person with no resistance (immunity) to the polio virus, resulting in infection from person to person. Most people who are infected with the polio virus are asymptomatic and gain lifelong protection (lifelong immunity). In some people who experience symptoms,

the viral infection spreads via the blood to the brain and spinal cord, thereby causing paralysis. Out of 100 children infected with the polio virus, 5-10 experiences symptoms like those of the common cold, accompanied by fever, and followed by headache and vomiting.

About 1 of 1,000-2,000 people infected with the polio virus experiences paralysis of the limbs. Some are permanently paralyzed or suffer from progression of symptoms, sometimes dying of respiratory distress.

(2) Diphtheria-pertussis-tetanus and inactivated polio vaccine (DPT-IPV), Diphtheria-pertussis-tetanus vaccine (DPT), and diphtheria-tetanus vaccine (DT) (inactivated vaccine)

The phase 1 initial vaccination is given after 2 months of age, in three doses in the case of DPT-IPV and DPT, with an interval of at least 20 days with the standard interval being 20 to 56 days. If the DT vaccine is used, it is to be delivered in two doses no earlier than 3 months after birth. The phase 1 booster is given at least 6 months (usually 1 year to 1 year and 6 months) after the completion of the initial vaccination. Take care not to miss a vaccination, as multiple injections are required. Phase 2 vaccination is given once at the age of 11-12 years using DT.

Although a voluntary vaccination, it is also possible to have your child receive the DPT vaccine at this time, strengthening their immunity to pertussis.

To acquire sufficient immunity, your child must be vaccinated according to fixed intervals. However, even in the event the interval between injections becomes longer than that specified, there are several methods which can be taken, so please consult with your family doctor and the municipal office.

The DPT-IPV can be used even with children who have already contracted one or more of pertussis, diphtheria, poliomyelitis (acute poliomyelitis), or tetanus.

In November 2012, the combined DPT (diphtheria, pertussis, tetanus) and IPV (inactivated polio) quadruple vaccines Quattrovac® (produced by KM Biologics) and Tetrabik® (produced by the Research Foundation for Microbial Diseases of Osaka University) were introduced to the market. In December 2015, the DPT-IPV quadruple vaccine, Squarekids® subcutaneous injection syringe (produced by Daiichi Sankyo Vaccine Co., Ltd.), was introduced to the market. However, the marketing of Squarekids® subcutaneous injection syringe (Daiichi Sankyo Vaccine Co., Ltd.) was discontinued in March 2021.

The incidence of serious cases (cases deemed to be serious by the reporter) among suspected cases of adverse reactions (adverse events) reported by medical institutions was 0.0012% for the DPT-IPV, 0.0017% for the DPT vaccine and 0.0002% for the DT vaccine. (The incidence reported from April 1, 2013 to September 30, 2023. Source: January 2024 documents 2-16, 2-11 and 2-12 from the 100th Working Group Meeting on Adverse Events, the Subcommittee

on Vaccination and Vaccines of the Health Sciences Council.)

Even in the absence of a serious adverse reaction, if your child is cranky or swelling occurs, consult with a doctor.

Although the incidence of diphtheria, pertussis, tetanus, and polio (acute poliomyelitis) has decreased, these diseases are all associated with serious complications, disabling sequelae, or even death. Therefore, it is recommended to receive vaccination for their prevention.

(3) Polio vaccine (inactivated vaccine)

An oral polio vaccine (OPV) had been used to eradicate polio in Japan and this state had been maintained up until August 2012; however, the OPV was replaced with an inactivated poliovirus vaccine (IPV) as a routine vaccination on September 1, 2012 in order to avoid vaccine-associated paralytic poliomyelitis (VAPP), a rare but serious adverse reaction to the OPV which develops in about one out of one million vaccine recipients. The IPV IMOVAX POLIO® subcutaneous injection (produced by Sanofi K.K.) has been used since September 2012. The quintuple vaccine against diphtheria, pertussis, and tetanus as well as polio (DPT-IPV, produced by KM Biologics and the Research Foundation for Microbial Diseases of Osaka University) have been used since November 2012.

The IPV includes antigens of three types of polio viruses (I, II and III). Resistance (immunity) to these three types of polio viruses reaches almost 100% with three IPV vaccinations; however, the fourth vaccination is needed because IPV maintains immunocompetence for a shorter time than the OPV.

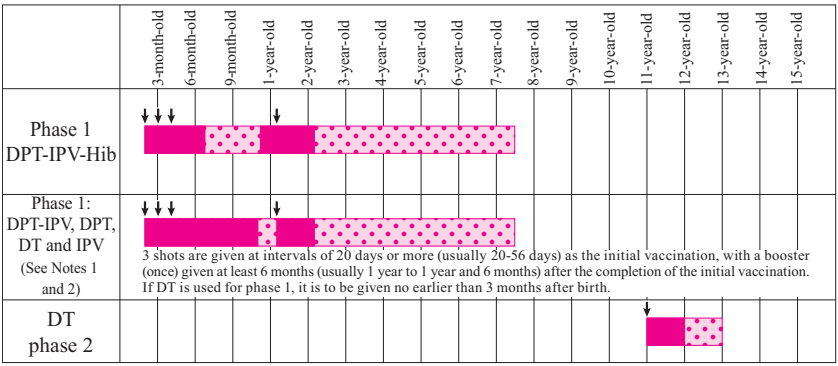
A domestic clinical trial of IMOVAX POLIO® showed that pain (18.9%), erythema (77.0%), swelling (54.1%), fever of 37.5˚C or more (33.8%), drowsiness (35.1%), and irritability (41.9%) were observed after the third vaccination. Precautions of shock and anaphylaxis (frequency unknown) and against convulsions as they were observed in 1.4% are described in the package insert. (See package insert [3rd ver.] revised in April 2023).

The incidence of severe cases (cases deemed to be serious by the reporter) among suspected cases of adverse reactions (adverse events) reported by medical institutions was 0.0010%. (The incidence reported from April 1, 2013 to September 30, 2023. Source: January 2024 document 2-15 from the 100th Working Group Meeting on Adverse Events, the Subcommittee on Vaccination and Vaccines of the Health Sciences Council.)

The switch from OPV to IPV is taking place all over the world. However, there are many cases that OPV-derived viruses (circulating vaccine derived Polio, virus: cVDPV) still lurking in sewage and river water infect non-vaccinated individuals and cause paralysis in regions where vaccination rates are low. As cases of OPV-derived virus infection have recently been reported in the United States, Israel, the United Kingdom, and Indonesia, there is a need to

improve polio vaccination coverage in these countries. In Japan, the DPT-IPV vaccination rate is high, and cVDPV has not been detected, so the risk is extremely low. However, there is a possibility that the virus will be brought into Japan from overseas, so it is recommended to receive a vaccine containing IPV.

(4) Vaccination schedule



Note 1: The DPT-IPV, DPT, and DT can also be given to children who have already experienced pertussis. If DT is used, it is to be delivered in two doses with the initial injection given no earlier than 3 months after birth. The DPT-IPV, DPT, and DT can also be given to children who have already experienced any of the diseases of diphtheria, tetanus, or polio.

Note 2: In the phase 1 initial vaccination, the same type of vaccine is usually given the required number of times.

◆ Tuberculosis

(1) Cause and course

Tuberculosis is caused by infection from Mycobacterium tuberculosis. The number of tuberculosis patients has markedly decreased in Japan, and the number of new cases in 2022 was 8.2 cases/100,000 population, falling below the WHO standard for low tuberculosis incidence (10.0 cases/100,000 population). However, tuberculosis can be transmitted to children from adults. Immunity against tuberculosis cannot be acquired in the womb, so newborn babies are also at risk of contracting the disease. Infants and children have low immunity against tuberculosis; as a result, they sometimes contract systemic tuberculosis or tuberculous meningitis, resulting in severe secondary complications.

It is recommended to receive a BCG vaccination within 1 year after birth as the BCG vaccine has the effect of preventing serious tuberculosis, such as meningitis and miliary tuberculosis, in infants.

The standard vaccination period is from 5 to 8 months after birth.

(2) BCG vaccine (live vaccine)

The BCG vaccine is made from attenuated Mycobacterium bovis.

The method used to administer the BCG vaccination in Japan is a percutaneous injection using an apparatus with multiple needles that is pressed into two locations on the upper arm. The vaccine should not be given elsewhere on the body due to possible adverse reactions, including keloid formation. The vaccination site should be allowed to dry away from light for about 10 minutes.

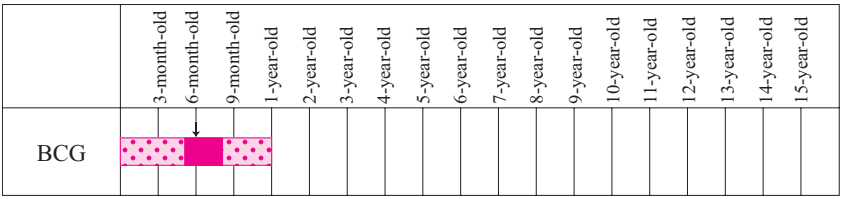
Red pockmarks appear on the vaccination site around 10 days after vaccination, and some may discharge a small amount of pus (fester). This reaction peaks about 4 weeks after vaccination; subsequently, the pockmarks are covered with scabs and heal completely by three months after vaccination, leaving only tiny scars. This scarring is not an abnormal reaction but evidence that a person has acquired immunity through the BCG vaccination. As the vaccination site will heal naturally, keep it clean and do not cover it with a bandage or plaster. However, if the vaccination site is still oozing three months after vaccination, please consult a doctor.

One rare adverse reaction is swelling in the lymph nodes below the armpit on the same side as the vaccination. This reaction can generally be left untreated; however, occasionally the area can grow tender, severely swollen, or, rarely, may fester and naturally tear. Should such a reaction occur, please consult a doctor.

The incidence of severe cases (cases deemed to be serious by the reporter) among suspected cases of adverse reactions (adverse events) reported by medical institutions was 0.0028%. (The incidence reported from April 1, 2013 to September 30, 2023. Source: January 2024 documents 2-20 from the 100th Working Group Meeting on Adverse Events, the Subcommittee on Vaccination and Vaccines of the Health Sciences Council.)

In cases where a child is infected with tuberculosis due to transmission from a family member etc., within 10 days of the injection the vaccination site may show an inflammatory reaction called Koch's phenomenon (redness, swelling, and suppuration at the vaccination site, generally followed in 2 to 4 weeks by decreased redness, swelling, and inflammation, after which the wound scarifies [leaves a scar] and heals). Unlike the usual reaction time (generally about 10 days after vaccination), the Koch phenomenon appears at an early stage, within several days of vaccination. If your child develops a reaction which suggests the Koch phenomenon, promptly consult your municipality or a physician, as your child may require treatment. In such cases, family members and other individuals close to the child who may have transmitted tuberculosis will also require a medical examination.

(3) Vaccination schedule



◆ Measles and rubella

(1) Cause and course

(1) Measles

Measles is caused by infection by the measles virus. Measles is highly contagious and spreads not only through droplets and contact but also through airborne transmission. Without vaccination, many people will contract the disease and there is risk of an epidemic. The main symptoms of prototypical measles are fever, cough, runny nose, bloodshot eyes, eye discharge, and rash. For the first 3 to 4 days, patients have a fever of 38˚C, which appears to decline but increases again to 39˚C to 40˚C, with a rash over the entire body. The fever goes down within 3 to 4 days, and the rash gradually disappears. The parts affected by the rash may remain darker for a while.

The main complications are bronchitis, pneumonia, otitis media, and encephalitis. About 7 to 9 out of 100 people with measles also get otitis media and about 1 to 6 get pneumonia. 1 to 2 out of 1,000 experiences encephalitis. One or two out of 100,000 measles patients develops subacute sclerosing panencephalitis (SSPE), a chronic progressive form of encephalitis.

A serious disease, even in advanced countries with sophisticated medical care, around 1 out of 1,000 measles patients dies. In Japan, approximately 20 to 30 people died annually during the epidemic which occurred in the years around 2000. Globally, cases of measles are once again on the rise, and many children, primarily in developing countries, die from measles.

● Airborne infection (droplet nuclei infection)

With an airborne infection, the virus or bacterium is discharged into the air and infects people in open spaces. Measles, varicella (chickenpox), and tuberculosis are airborne diseases.

(2) Rubella

Rubella is caused by the rubella virus and is spread by droplet and contact transmission. The incubation period is 2 to 3 weeks. Prototypical rubella develops with mild cold-like symptoms, and the main symptoms are rash, fever, and posterior cervical lymphadenopathy (lymph nodes swelling in the back of the throat). Conjunctival congestion also occurs. Older children and adults experience a high frequency of arthritis. The prognosis is generally good, but thrombocytopenic purpura and encephalitis may also be observed, and, rarely, hemolytic anemia. According to the National Epidemiological Surveillance of Infectious Diseases, during the rubella outbreak from 2018 to 2019 (with a total of 5,239 cases), there were 21 reported cases of thrombocytopenic purpura and 2 reported cases of encephalitis. Adult patients experience severe symptoms.

When a pregnant woman is infected by the rubella virus before around the 20th week of pregnancy, there is a very high risk of her infant being born with congenital rubella syndrome which may include heart abnormalities, cataracts, hearing impairment, and delayed growth and development.

(2) Combined measles-rubella (MR) vaccine, measles (M) vaccine, rubella (R) vaccine (live vaccine)

The MR live vaccine contains attenuated measles and rubella viruses.

Once your child turns 1 year old, you should have him or her receive the phase 1 vaccination as soon as possible.

Both the measles and rubella vaccines give 95% or more of children immunity after one injection, but out of caution in case of non-response to the first dose and to prevent age-related decline of immunity, a second injection (phase 2 vaccination) is now performed.

Even if your child received the measles and rubella vaccine before his or her first birthday, it is not counted in the number of vaccinations received because vaccination under one year of age is insufficient for acquiring immunity. Have him or her receive the routine phase 1 vaccination once he or she turns 1 year old, and the phase 2 vaccination once the appropriate age is reached.

Eligibility for the phase 2 vaccination is the year before admission into elementary school,

that is, children in their final year of kindergarten or nursery school.

For the phase 1 and 2 vaccinations, the combined measles-rubella (MR) vaccine is used.

The combined measles-rubella (MR) vaccine can also be used for individuals who have already contracted measles or rubella.

If your child has received a gamma globulin injection for the purpose of treating or preventing illness, please consult your physician for the appropriate timing of vaccination.

The data concerning adverse reactions to the measles and the rubella vaccines shows that anaphylaxis, thrombocytopenic purpura, encephalitis, and seizure may occur rarely.

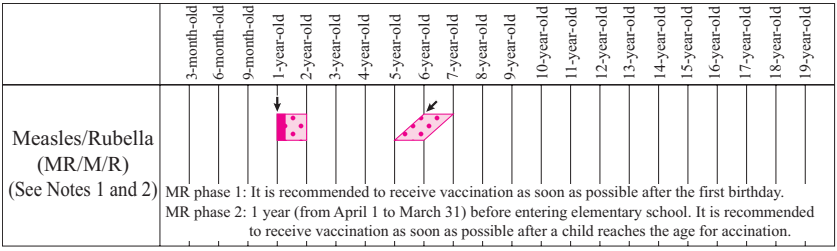
Febrile seizures (seizures caused by a fever) have occasionally (about 1 child in 300 children) been reported after measles vaccination. In addition, there have been reports of children experiencing encephalitis/encephalopathy in extremely rare cases (1 child or less in 1-1.5 million children).

The incidence of severe cases (cases deemed to be serious by the reporter) among suspected cases of adverse reactions (adverse events) reported by medical institutions was 0.0010%. (The incidence reported from April 1, 2013 to September 30, 2023. Source: January 2024 document 2-1 from the 100th Working Group Meeting on Adverse Events, the Subcommittee on Vaccination and Vaccines of the Health Sciences Council.)

Although the rubella vaccine is a live vaccine and the rubella virus multiplies in the body similarly to the measles vaccine, a vaccinated person does not infect those around him or her.

Measles causes severe symptoms and may result in sequelae or death. When a pregnant woman contracts rubella, her infant may be born with congenital rubella syndrome which may include heart abnormalities, cataracts, retinopathy, hearing impairment, and intelligence impairment. Make sure you are vaccinated so as to prevent contracting these diseases or transmitting them to others.

(3) Vaccination schedule



Note 1: A simultaneous vaccination for measles and rubella in phase 1 and 2 is given using the combined measles-rubella (MR) vaccine.

Note 2: Individuals who have experienced either measles or rubella before can receive the vaccine for the disease they have not experienced or the measles-rubella (MR) vaccine and are normally given the MR vaccine.

* Men born between April 2, 1962 and April 1, 1979 have been added to the list of those eligible for routine vaccination concerning rubella (phase 5 routine vaccination for rubella).

◆ Varicella (chickenpox)

(1) Cause and course

Varicella (chickenpox) is an acute infectious disease caused by initial infection with the varicella-zoster virus (“VZV”). It is one of the most infectious diseases, spread by direct contact, droplets, and airborne infection. Once a person is infected, the virus remains dormant in the body (in the trigeminal ganglia and other cerebral ganglia, and in the dorsal root ganglia) and reactivates to cause herpes zoster (shingles) when the person ages, or when the immune system is compromised.

The incubation period of varicella (chickenpox) is generally about 2-3 weeks (10-21 days). The main symptom of prototypical varicella (chickenpox) is a characteristic rash with itching. There may also be a fever. The rash begins as raised red spots, progressing in 3 or 4 days to blisters that crust over and form scabs before healing. Although the rash tends to be distributed on the abdomen, back, and face, it also characteristically appears on the scalp and other parts which are covered with hair.

Varicella usually clears spontaneously in about 1 week, but in rare cases it can be accompanied by encephalitis, pneumonia, or liver function abnormality. Antiviral medication (e.g. Acyclovir) is sometimes used. It is not unusual for bacterial infections to develop via the skin and lead to purulence. In some cases, complications such as sepsis and other severe bacterial infections may occur. High-risk patients (patients with malignant tumors such as acute leukemia or patients who are or may be immunosuppressed due to treatment) are particularly likely to develop severe symptoms.

In accordance with regulations such as the Enforcement Regulations for the School Health and Safety Act, children are to refrain from attending nursery school, kindergarten, or elementary/middle/high school until all of the rash has crusted over (formed scabs).

When adults develop varicella (chickenpox), symptoms tend to become more severe compared to children.

(2) Varicella (chickenpox) vaccine (live vaccine)

This is a live vaccine containing attenuated VZV. It was developed in Japan ahead of the rest of the world. About 20% of the individuals who receive this vaccine once experience varicella (chickenpox) later, but in a milder form. The vaccine is given twice to ensure that infection does not occur.

It has been shown that vaccine administration within 3 days of exposure to a varicella patient is effective in preventing disease. This kind of vaccination is also used to prevent hospital-acquired infection.

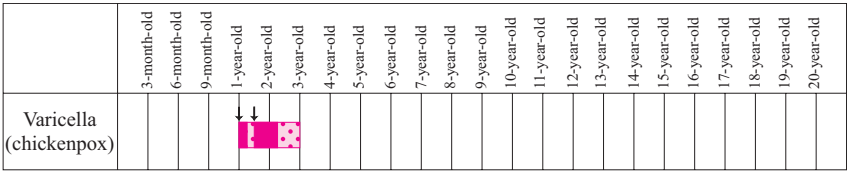
Almost no adverse reactions are observed in healthy children and adults; however, fever and rash occasionally develop, and local redness, swelling (puffiness), and induration (stiffness)

are observed in rare cases. High-risk patients (patients who may be immunosuppressed due to the effects of treatment for acute lymphatic leukemia or nephrotic syndrome) may receive the vaccination, provided that certain conditions are met. However, the patient may develop a fever with raised red spots and blisters 14 to 30 days after vaccination. (See package insert [3rd ver.] revised in January 2022)

The incidence of severe cases (cases deemed to be serious by the reporter) among suspected cases of adverse reactions (adverse events) reported by medical institutions was 0.0010%. (The incidence reported from April 1, 2013 to September 30, 2023. Source: January 2024 documents 2-5 from the 100th Working Group Meeting on Adverse Events, the Subcommittee on Vaccination and Vaccines of the Health Sciences Council.)

After being made a routine vaccination on October 2014, the incidence of varicella (chickenpox) decreased dramatically. The varicella vaccine can be given at the same time as the MR vaccine. Children aged 12 months to no later than 36 months are given a freeze-dried live attenuated varicella vaccine, with the first injection given when the child is 12 months to no later than 15 months and the second injection given after an interval of at least 3 months with the standard interval being between 6 to 12 months. Children who already received the varicella vaccine as a voluntary vaccination are deemed to have received the number of injections he or she has already undergone.

(3) Vaccination schedule



◆ Japanese encephalitis

(1) Cause and course

Japanese encephalitis is caused by the Japanese encephalitis virus. The Japanese encephalitis virus is transmitted by mosquitoes carrying viruses that have multiplied in pigs and other hosts. After an incubation period of 7 to 10 days, it may develop into acute encephalitis with symptoms such as high fever, headache, vomiting, disturbance of consciousness, and convulsions. Japanese encephalitis does not spread from person to person.

One in 100-1,000 people infected with the virus develops encephalitis, etc. Some people develop meningitis, while others may only experience symptoms like a summer cold. The fatality rate of encephalitis is about 20-40%, but many people suffer from nervous system sequelae after recovering from the disease.

In Japan, the disease occurs mainly in the western areas, but the Japanese encephalitis virus is found throughout the nation and especially in western Japan. Japanese encephalitis outbreaks among domesticated pigs occur yearly from June to around October, during which time approximately 80% of pigs are infected in some geographical areas. In the past, the disease was prevalent among small and school-age children, but due to the wider use of vaccination and changes in living environments, the number of patients has decreased. In recent years, patients have mostly been elderly, but in 2015, a 10-months old infant in Chiba prefecture was determined to have Japanese encephalitis. There were also 11 reported incidents in 2016, mostly in elderly people. This was the first time the number of patients exceeded 10 per year since 1992. As of December 3, 2023, 6 incidents have been reported. (Source: Infectious Diseases Weekly Report, National Epidemiological Surveillance of Infectious Diseases, by the National Institute of Infectious Diseases, Week 48, 2023)

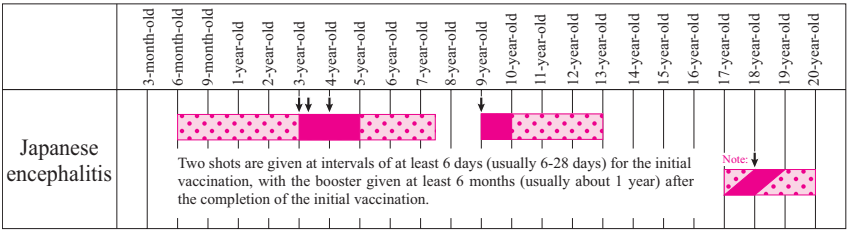
(2) Freeze-dried Japanese encephalitis vaccine (inactivated vaccine)

The freeze-dried cell culture-derived Japanese encephalitis vaccine in use in Japan today is created by growing the virus in Vero cells and killing (inactivating) the virus with a substance such as formalin, after which it is refined.

The incidence of severe cases (cases deemed to be serious by the reporter) among suspected cases of adverse reactions (adverse events) reported by medical institutions was 0.0007%. (The incidence reported from April 1, 2013 to September 30, 2023. Source: January 2024 documents 2-21 from the 100th Working Group Meeting on Adverse Events, the Subcommittee on Vaccination and Vaccines of the Health Sciences Council.)

Eligibility for the phase 1 routine vaccination is children between 6 and 90 months after birth. The standard schedule is to give two injections separated by an interval of 6 to 28 days from the day the child turns 3 and before his or her fourth birthday, and one injection from the fourth birthday to before the child turns 5. Eligibility for the phase 2 routine vaccination is children from 9 years to before he or she turns 13. The standard schedule is to give one injection between the child's ninth and tenth birthdays.

(3) Vaccination schedule



Note: Persons born between April 2, 1995 and April 1, 2007 who were unable to receive the phase 1 and 2 vaccine are able to receive the vaccine as a routine vaccination if under the age of 20.

(4) Special consideration for vaccination (to secure opportunities for vaccination for children who were unable to receive the vaccine due to suspension of active recommendation in 2005)

Persons under the age of 20 who were born between April 2, 1995 and April 1, 2007 and who may not have received the phase 1 (three injections) and phase 2 (one injection) vaccine due to suspension of active recommendation on May 30, 2005 are eligible for the following measures to secure opportunities for vaccination.

(1) Persons who need 3 injections remaining of phase 1 and 2 (persons who received 1 injection of the initial vaccination in phase 1 [persons who received the first injection]) are to be given 2 injections of freeze-dried cell culture-derived Japanese encephalitis vaccine separated by an interval of at least 6 days, with the fourth injection for persons at least 9 years of age to be given after an interval of at least 6 days following the third injection.

(2) Persons who have 2 injections remaining of phase 1 and 2 (persons who received two injections of the initial vaccination in phase 1 [persons who received the second injection]) are to be given the third injection of freeze-dried cell culture-derived Japanese encephalitis vaccine after an interval of at least 6 days, with the fourth injection for persons at least 9 years of age to be given after an interval of at least 6 days following the third injection.

(3) Persons who are to receive phase 2 of the vaccination (persons who have completed phase 1 injections [persons who received the third injection]) are to be given the fourth injection for persons at least 9 years of age after an interval of at least 6 days following the third injection.

(4) Persons who have not received any of the phase 1 and 2 vaccinations are to be given freeze-dried cell culture-derived Japanese encephalitis vaccine with two (i.e., first and second) injections separated by an interval of at least 6 days (usually 6 to 28 days), followed by 1 booster at least 6 months (usually about 1 year) after the second injection (i.e., third injection), with the fourth injection for persons at least 9 years of age to be given with one shot after an interval of at least 6 days after the third injection.

Because there was insufficient recommendation of phase 2 vaccination for persons who will turn 18 between 2017 and 2024 (persons born between April 2, 1999 and April 1, 2007) due to suspension of active recommendation from May 30, 2005 to March 31, 2010, the measures in (4) were adopted for the purpose of active recommendation of the vaccine to persons turning 18 in every applicable year.

A pregnant or possibly pregnant woman aged 13 years or more is not allowed to receive vaccination in principle and can receive vaccination only if the advantage of vaccination is confirmed to be superior to the risk.

You can ask questions on vaccination and receive latest information from your municipality. A Q&A is available from the website of the Ministry of Health, Labour and Welfare: "Q&A on Japanese encephalitis vaccination" (Japanese) (https://www.mhlw.go.jp/bunya/kenkou/kekkakukansenshou21/dl/nouen_qa.pdf).

◆Human papillomavirus infection (protection against cervical cancer)

(1) Cause and course

The human papillomavirus (HPV) is a common virus which infects many people, of whom some women develop cervical cancer. Out of the more than 100 types of HPV, types 16 and 18 are considered to be causal for approximately 50 to 70% of cases of cervical cancer. Most HPV infections clear spontaneously and the virus becomes undetectable. However, in some women, over the course of several years to several decades, precancerous lesions and then cervical cancer will develop. Every year, about 11,000 women develop cervical cancer in Japan, and an estimated 2,900 die from the disease (source: "Cancer Information Service," Center for Cancer Control and Information Services, National Cancer Center). In addition to vaccines to prevent HPV infection, early detection and early treatment of precancerous lesions through cervical cancer screening tests hold promise for decreasing incidence and mortality rates of this disease.

(2) HPV vaccine

Vaccines to prevent cervical cancer that are available as routine vaccinations in Japan are a bivalent vaccine (Cervarix®) containing antigens of the HPV type 16 and 18 viruses, which are most frequently detected from domestic and foreign patients with cervical cancer, and a tetravalent vaccine (Gardasil®) containing antigens of the type 6 and 11 viruses which are causes of condyloma acuminatum and recurrent respiratory papillomatosis. A 9-valent vaccine (Silgard® 9) which also protects against types 31, 33, 45, 52, and 58 was also approved and in April 2023 was included in the routine vaccination program. In foreign studies of persons not infected with HPV, each vaccine has been shown to be highly effective in preventing both infection and precancerous lesions. Therefore, countries are recommending that the vaccination be given to young people before their first sexual contact.

Adverse reactions described in domestic package inserts include local reactions such as pain (83-98%), redness (30-85%) and swelling (25-81%) at the injection site; and systemic reactions including slight fever (3-6%) and malaise; however, most of these are transient and disappear (see the following package inserts: Cervarix® [1st ver.] revised in December 2023; Gardasil® [1st ver.] revised in March 2023; Silgard® 9 [1st ver.] revised in March 2023).

The incidence of serious cases (cases deemed to be serious by the reporter) among suspected cases of adverse reactions (adverse events) reported by medical institutions was 0.0079% for

Cervarix, 0.0054% for Gardasil and 0.0006% for Silgard 9. (The incidence reported from the start of sales to September 30, 2023. Source: January 2024 documents 2-8, 2-9 and 2-10 from the 100th Working Group Meeting on Adverse Events, the Subcommittee on Vaccination and Vaccines of the Health Sciences Council.)

Vaccinated persons still need routine cervical cancer screening because the vaccine may not always provide sufficient immunization and does not protect against all HPV types which cause cervical cancer.

(1) When using the bivalent vaccine for the prevention of human papillomavirus infection, the standard vaccination period is from the first to the final day of the year in which the individual turns 13. The standard schedule is to give 2 injections separated by an interval of 1 month, followed by another injection after an interval of at least 6 months after the first injection. If said schedule cannot be followed, 2 injections are given separated by an interval of at least 1 month, followed by 1 injection after an interval of at least 5 months after the first injection, and 2.5 months after the second injection.

(2) When using the tetravalent vaccine for the prevention of human papillomavirus infection, the standard vaccination period is from the first day to the last day of the fiscal year in which the individual turns 13. The standard schedule is to give 2 injections separated by an interval of 2 months, followed by another injection after an interval of at least 6 months after the first injection. If said schedule cannot be followed, 2 injections are given separated by an interval of at least 1 month, followed by 1 injection after an interval of at least 3 months after the second injection.

(3) When using the 9-valent vaccine for the prevention of human papillomavirus infection, the standard vaccination period is from the first day to the last day of the fiscal year in which the individual turns 13. One of the two schedules shown below is to be followed (the schedule shown in A is to be followed only when giving the vaccine to an individual between the first day of the fiscal year in which the individual turns 12 and the date the individual turns 15 at the time of the first injection).

   a) The standard schedule is to give 2 injections separated by an interval of 6 months. If said schedule cannot be followed, 2 injections are given separated by an interval of at least 5 months.

   b) The standard schedule is to give 2 injections separated by an interval of 2 months, followed by another injection after an interval of at least 6 months after the first injection. If said schedule cannot be followed, 2 injections are given separated by an interval of at least 1 month, followed by 1 injection after an interval of at least 3 months after the second injection.

(4) In general, the same human papillomavirus vaccine formulation should be used to complete the series, if possible. However, in light of a certain level of evidence indicating the safety and immunogenicity of the bivalent, quadrivalent, or 9-valent vaccine administered to the same individual, municipalities may, in the event of circumstances deemed unavoidable, conduct the rest of the series following one of the two schedules shown below for individuals who have been given the bivalent or quadrivalent vaccine for their first or second injections.

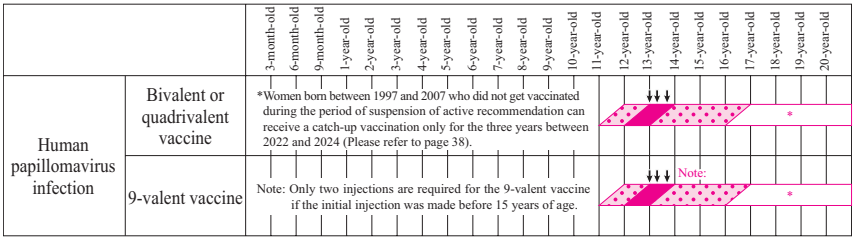
a) An individual given the bivalent or quadrivalent vaccine for their first injection is given 1 intramuscular injection of the 9-valent vaccine after an interval of 2 months from the first injection, followed by 1 injection of the same vaccine after an interval of 6 months from the first injection. However, if said schedule cannot be followed, the individual is given 1 intramuscular injection of the 9-valent vaccine after an interval of 1 month from the first injection, with the second and subsequent injections given intramuscularly using the same vaccine after an interval of at least 3 months.

b) An individual given the bivalent or quadrivalent vaccine for their first and second injections is given 1 intramuscular injection of the 9-valent vaccine after an interval of 6 months from the first injection. However, if said schedule cannot be followed, the individual is given 1 intramuscular injection of the 9-valent vaccine after an interval of at least 3 months from the second injection.

(5) In regard to catch-up vaccination, if the type of human papillomavirus-like particle vaccine given in the past is unknown, the choice of which vaccine to give should be made upon consultation between the vaccine recipient and the doctor of the medical institution conducting the vaccination.

(6) Syncope, a vasovagal reaction, sometimes occurs after vaccination against human papillomavirus infection. Therefore, to prevent fainting due to syncope, a child who has been vaccinated should be seated and observed, and the child should be instructed not to stand if possible, for 30 minutes after injection.

(3) Vaccination schedule



(4) Routine HPV vaccination

At the June 14, 2013 joint meeting of Working Group Meeting on Adverse Events, the Subcommittee on Vaccination and Vaccines of the Health Science Council and the Subcommittee on Drug Safety of the Committee on Drug Safety in the Pharmaceutical Affairs and Food Sanitation Council, it was set forth that "due to sustained pain whose relationship with the vaccine cannot be ruled out being observed after vaccination with the HPV vaccine, the routine vaccination should not be actively recommended until the frequency of onset of this adverse reaction is further elucidated and appropriate information can be provided to citizens," and the decision was made by the Ministry of Health, Labour and Welfare to suspend active recommendation of the vaccination. After that, since November 2021, at the same meeting, it has been discussed how to evaluate the efficacy and safety of HPV vaccines, how to deal with the symptoms that occur after HPV vaccination, and how to provide information about HPV vaccines. In conclusion, it was confirmed that there were no particular concerns about safety, and that the efficacy of vaccination clearly outweighed the risk of adverse reactions. Then, in November 2021, a notice was issued to end "the suspension of active recommendation." In December 2021, a notice was issued stating that vaccination shall be provided temporally beyond the target age of conventional routine vaccinations (hereinafter referred to as "catch-up vaccinations") as a measure for those who missed the opportunity of vaccination due to the suspension of active recommendation. The Preventive Vaccination Law Enforcement Ordinance (Cabinet Order No. 197 of 1948) was revised and came into effect on April 1, 2022.

From the viewpoint of ensuring a fair vaccination opportunity for those who missed the vaccination opportunity due to the suspension of active recommendation, the vaccination shall be provided beyond the target age of the conventional routine vaccination as follows.

Target of catch-up vaccinations	Females born in 1997 to 2007 who were subject to the routine vaccination during the period of suspension of active recommendation (Females born in 2006 will be subject from 2023, and females born in 2007 will be subject from 2024).
Target period	Three years from April 2022 to March 2025

*In response to the Cabinet Order for Partial Revision to the Preventive Vaccination Law Enforcement Ordinance (Cabinet Order No. 105 of 2022), it came into effect on April 1, 2022.

For more information on the safety and efficacy of the HPV vaccines, please refer to the brochure on the HPV vaccines posted on the Ministry of Health, Labour and Welfare website (https://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou28/index.html). For details on how to operate catch-up vaccinations, please check the latest information from the Ministry of Health, Labour and Welfare and your municipality.

Note that the WHO and the Japanese Medical Society have positioned HPV vaccination as a "vaccine necessary to protect women from cancer." In Japan, indication to males was added only in the tetravalent HPV vaccine in December 2020, and males aged 9 has been subject (voluntary vaccination).

8. What to do if your child experiences an adverse reaction to a vaccination

(1) Normally observed reactions

Depending on the type of vaccine, fever, redness, swelling (puffiness), and induration (stiffness), and rashes at the injection site occur fairly often. In many cases, these symptoms disappear within several days and are not a cause for concern.

(2) Serious adverse reactions

If your child has severe swelling at the vaccination site, or has fever or seizures after vaccination, consult a doctor. If your child's symptoms meet the criteria for reporting adverse reactions after vaccination, the doctor will inform the Pharmaceuticals and Medical Devices Agency (PMDA).

Although adverse reactions depend on the type of vaccine, vaccination extremely rarely (about one in several million people) causes serious adverse reactions, such as encephalitis

and neuropathy. Such cases will be evaluated on the basis of Japan's basic approach in regard to relief programs, namely that "rigorous medical causation is not imperative and that relief shall also apply in cases where the possibility of symptoms which appeared after inoculation having been caused by the vaccination cannot be ruled out." On this basis, the patient is considered eligible for compensation for injury to health under the Preventive Vaccination Law if the Minister of Health, Labour and Welfare gives authorization.

(3) Coincidental reactions

Symptoms that occur soon after vaccination are often thought to have been caused by vaccination. However, sometimes these symptoms are caused by another infection that happens to develop simultaneously. This is then called a "coincidental reaction."

(4) Aid system for people with impaired health due to vaccination

(1) A person who has an adverse reaction due to routine vaccination or provisional vaccination and whose ability to perform daily activities is impaired due to injury to health can be compensated by the government according to the Preventive Vaccination Law.

(2) The compensation consists of payment of medical expenses, medical benefits, an annuity for disabled children, a disability annuity, lump-sum death benefits, and funeral expenses, all of which are designated by law according to the severity of the injury to health. All compensation, except lump-sum death benefits and funeral expenses, is continually paid until the completion of treatment or improvement in the injury to health.

(3) Compensation is paid to the patient after the relevant injury has been certified to be caused by vaccination by a governmental review committee comprising specialists in vaccination, infection medicine, law, and related disciplines, who discuss the causal relationship of the relevant injury with vaccination, i.e., whether the relevant injury was caused by vaccination or other factors (infection before or after vaccination, or other causes).

(4) When vaccination is desired after the designated period for routine or provisional vaccination, said vaccination is considered not to be controlled under the Preventive Vaccination Law (voluntary vaccination). In the event a child is injured by vaccination in this situation, he/she will receive compensation according to the Pharmaceuticals and Medical Devices Agency Law; however, the subject and the amount of compensation differ from those of the Preventive Vaccination Law.

* In the event you need to submit an application for compensation, consult with your municipal office in charge of vaccination.

* The following topics are quoted from the "Vaccination Guidelines 2024 Version" from the Public Foundation of Vaccination Research Center regarding COVID-19 vaccination.

[Reference 1] Novel coronavirus (COVID-19) infection

(1) Overview of the disease

An outbreak of unexplained pneumonia in Wuhan City, Hubei Province, China at the end of December 2019 was reported. On January 9, 2020 it was announced that the causative virus was a new coronavirus. The international name of the disease was announced as COVID-19 and the causative virus was designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). With the virus expected to spread rapidly to other countries across the world, the World Health Organization (WHO) declared the situation a Public Health Emergency of International Concern (PHEIC) on January 30 and characterized the outbreak as a pandemic on March 11.

In Japan, COVID-19 was specified on January 28, 2020 as a "Designated Infectious Disease" according to the Infectious Diseases Control Law. In terms of the School Health and Safety Act, it was deemed to be equivalent to Category 1 on the basis of the Infectious Diseases Control Law. On March 13, the Act on Special Measures against Novel Influenza, etc., was amended to stipulate that measures against COVID-19 would be taken on the basis of this Act. On December 9, 2020, COVID-19 became a target for provisional vaccination. Subsequently, Japan faced roughly 8 waves of COVID-19 by May 2023. COVID-19 was classified as a Category 5 infectious disease starting on May 8, 2023, when the eighth wave showed signs of decrease. Accordingly, it was classified as a Category 2 disease under the School Health and Safety Act.

On May 5, 2023, the WHO declared that COVID-19 is no longer a PHEIC, although with a warning that it still remained a global threat.

Since the emergence of the Omicron strain, the incubation period has shortened to 2 or 3 days in most cases. The route of transmission is mainly by droplets, although aerosol transmission also occurs in closed spaces. Contact infection is possible but less frequent.

As it is a respiratory disease, the symptoms are mainly fever, sore throat, coughing, etc. When it first began to spread, pediatric cases were few and asymptomatic or mostly mild even in case of symptoms being present. However, infections in children have increased since the Omicron strain became predominant, with more cases developing febrile seizures and croup-like symptoms. Children under the age of 2 and persons with underlying conditions are considered

at risk for severe disease. Rates of severe disease and death are high in the elderly.

(2) Benefits of vaccination

Multiple reports from Japan and overseas are showing that vaccinating children is effective in preventing the onset, infection and severe illness from COVID-19. The Japan Pediatric Society recommends vaccinating children between 6 months and 17 years of age. In a U.S. study of the long-term effectiveness of vaccination, the primary series (2 injections) and booster were found to be effective in children aged 5-11 years, and the effectiveness of a bivalent vaccine booster dose in preventing onset of disease was reported to be 76.7% at 1 month after the injection. Reinfection may occur after recovery from the disease. It has been found that vaccination is associated with reduced likelihood of reinfection. For children aged 0-4 years, it has been reported that the onset prevention effect of primary vaccination (3 injections) is 63.8% at 2 months and 58.1% at 5 months after the first dose. In all age groups, effectiveness in preventing severe disease (hospitalization) was found to be higher than effectiveness in preventing onset of disease symptoms. In an overseas study of the efficacy of the vaccine in preventing deaths in children and young people aged 5-25, the effectiveness of the vaccine in preventing deaths during the Omicron period was 42% with 2 injections and 64.5% with the booster.

(3) Vaccine characteristics

Although COVID-19 vaccines were being developed in Japan and abroad, the first vaccine to be used for practical vaccination was an mRNA vaccine containing the mRNA of the SARS-CoV-2 spike protein encapsulated in lipid nanoparticles. Other vaccines in practical use include recombinant viral vector vaccines which use non-pathogenic viruses carrying SARS-CoV-2 spike protein, and live-attenuated vaccines. In Japan, the Pfizer mRNA vaccine was approved for marketing on February 14, 2021. Provisional vaccination under the Preventive Vaccination Law began on February 17 for healthcare personnel and on April 12 for the elderly. On May 21, 2021, the Takeda/Moderna mRNA vaccine and the AstraZeneca recombinant chimpanzee adenovirus vector vaccine were approved for marketing. At large-scale vaccination centers, vaccination using the Takeda/Moderna mRNA vaccine started on May 24, 2021 for the elderly, and workplace vaccinations started on June 21, 2021. Vaccination with the AstraZeneca vaccine ended at the end of September 2022.

In June 2021, vaccination of children aged 12 and over with the COVID-19 vaccine began. On January 21, 2022, the vaccine received regulatory approval for use in children aged 5 to 11 years, and was positioned as a product for a special provisional vaccination. Furthermore,

in October 2022, vaccinations for children aged 6 months to 4 years also started. In regard to the vaccine to be used for injections starting in autumn 2023, it was decided at the Meeting of the Subcommittee on Vaccination and Vaccines in June 2023, to use a monovalent vaccine containing the XBB.1 lineage.

COVID-19 vaccination will be conducted on a routine basis after COVID-19 is designated a Category B disease in FY2024. (Administrative Notice dated November 22, 2023 by Vaccination Division, Department of Infectious Disease Prevention and Control, Public Health Bureau, Ministry of Health, Labour and Welfare)

(4) Precautions for injection

As of the present, all of the COVID-19 vaccines are delivered intramuscularly.

Different COVID-19 vaccines and dosages are available depending on ages. A different formulation are approved in adults and children for certain vaccines (e.g., Pfizer mRNA vaccine). Therefore, it is necessary to check the vaccine recipient's age against the vaccine type in advance of injection.

At the 55th Meeting of the Subcommittee on Vaccination and Vaccines of the Health Sciences Council in February 2024, approval was given for the simultaneous injection of COVID-19 vaccine and another vaccine without an interval requirement when deemed necessary by a physician after FY 2024. These measures are similar to those for other vaccines except injectable live vaccines.

(5) Adverse reactions

A variety of symptoms including localized pain and swelling at the injection site, headache, and fever have been identified, but most are mild to moderate and short-term. No significant safety concerns have been identified from the information obtained to date. There are also reports indicating that the incidence of adverse reactions is lower in younger people. A U.S. analysis of various post-vaccination symptoms showed that myocarditis was reported in males aged 5-11 following the second dose, but that the reported incidence was lower compared to males aged 12-15 and 16-17. In a Japanese study, the incidence of myocarditis meeting the Brighton criteria levels 1-3 was 0.6 cases out of 1 million doses in children aged 5-11. No cases have been reported to date in children aged 0-4. In Japan, anaphylactic shock has been reported as a severe adverse reaction. Vaccine recipients should be observed for a minimum of 30 minutes after vaccination, and must seek medical attention in the event of symptoms such as chest pain, breathing difficulty, or lethargy within several days post-vaccination.

*This information is up to date as of February 2024. Routine vaccination (Category B) is scheduled to start in FY2024. For updates and details refer to information provided by MHLW.

[Reference 2] Diseases preventable by voluntary vaccination and overview of vaccines

Voluntary vaccination, which is not subject to the Preventive Vaccination Law, is conducted in consultation between a vaccine recipient (parents/guardians) and a doctor and is not promoted by the government; however, the vaccines used are approved by the Ministry of Health, Labour and Welfare under the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (Act on the Pharmaceuticals and Medical Devices Agency).

Voluntary vaccinations include vaccinations to prevent seasonal influenza (a routine vaccination for adults from 65 years), mumps, hepatitis A, yellow fever, rabies, tetanus, meningococcal disease, herpes zoster (shingles), and Mpox, and also refer to routine vaccinations when they are given outside the eligible age range or period.

The seasonal influenza and mumps vaccines that many children receive are explained below.

In the unlikely event a child is injured by a vaccination, he/she will receive compensation according to the Pharmaceuticals and Medical Devices Agency Law; however, the subject and the amount of compensation differ from those of the Preventive Vaccination Law (routine vaccination).

* In the event you need to submit the application for compensation, consult with your municipal office in charge of vaccination.

◇Seasonal influenza vaccine (inactivated vaccine, live intranasal vaccine)

The seasonal influenza vaccination for the elderly is designated as a routine vaccination by the Preventive Vaccination Law; that for children is considered a voluntary vaccination.

(1) Cause and course

Seasonal influenza is an acute respiratory infection which suddenly develops systemic symptoms including fever, chill, headache, and muscle pain. The incubation period is 24- 72 hours. Respiratory symptoms (stuffy nose, sore throat, and cough, etc.) often appear later. Patients without complications recover within 2-7 days. Complications, especially pneumonia and encephalopathy, are severe.

(2) Overview of vaccine

2 lineages of seasonal influenza type A (H1N1 and H3N2) and 2 of type B (Yamagata and Victoria) are injected into the chorioallantoic membrane of embryonated chicken eggs and allowed to multiply. After ether treatment to isolate the hemagglutinins on the viral surface, formalin inactivation is performed to obtain the vaccine. Decisions are made each year on which viral strains to include in the seasonal influenza vaccine, on the basis of epidemiological

and virological assessments.

Reports vary on the effectiveness of the influenza vaccine in infants and young children. In a 2015/16 season study in children under 6 years of age, the efficacy of the influenza vaccine in preventing disease was reported to be 60%. Influenza vaccines are considered to be effective to a certain extent in preventing the onset of disease as well as in preventing severe illness and death in the event symptoms develop. (Cited from MHLW website "Q&A on Influenza, 2023" Q21)

Embryonated chicken eggs are used in the manufacturing process of the seasonal influenza vaccine; however, the egg components are eliminated in the purification process. Nevertheless, caution is necessary when vaccinating persons with clear allergies to eggs. Persons who experience an anaphylactic reaction to chicken eggs and meat are asked to consult with a specialized facility if they wish to receive the vaccine.

The incidence of serious cases (cases deemed to be serious by the reporter) among suspected cases of adverse reactions (adverse events) reported by medical institutions was 0.00006%. (The incidence reported from October 1, 2022 to March 31, 2023. Source: July 2023 documents 2-26 from the 94th Working Group Meeting on Adverse Events, the Subcommittee on Vaccination and Vaccines of the Health Sciences Council.)

A live intranasal vaccine for children aged 2-18 will be launched in FY2024. For details, please refer to information updates as they are made available.

◇Mumps vaccine (live vaccine)

(1) Cause and course

Mumps is caused by the mumps virus and is spread by droplet or contact infection. The virus proliferates and spreads throughout the body, causing lesions in various internal organs. The viruses proliferate and spread over the body and cause lesions in various internal organs. The incubation period is 2-3 weeks. The period which an infected person may infect those around them is believed to be from several days before onset to 5 days after start of swelling of the parotid gland, submaxillary gland, or sublingual gland. The primary symptom is swelling of the parotid gland. The swelling is painful and exhibits indistinct borders. The submaxillary gland and/or sublingual gland may also develop swelling, and may also be accompanied by fever. When an older child or adult contracts the disease, the symptoms are marked and the frequency of complications is greater. The most frequently encountered complication is aseptic meningitis, at a diagnostic frequency of 1-10%. Although lower in frequency, other complications include encephalitis and pancreatitis. Adolescent and older men may also develop the complication of orchitis and women, oophoritis. Special caution is required for the difficult to treat complication of hearing loss.

(2) Overview of vaccine

This is a live vaccine containing attenuated mumps viruses. The post-inoculation seroconversion rate is high, at more than 90%, and in domestic outbreak investigation, the effect of the vaccine is believed to be about 80%. Most people who develop the disease despite being vaccinated generally experience a milder form of the disease. (Report by Mumps Vaccine Working Team of the Vaccination Working Group)

Possible adverse reactions to mumps vaccines available on the market include mild swelling of the parotid glands in 1% of the individuals who received this vaccine. The frequency of the adverse reaction of aseptic meningitis is stated to be about 1 in every 1,600-2,300 persons vaccinated (from vaccine package insert); however, although it has recently been reported that there are differences in frequency depending on the age of vaccination, it has been reported that the frequency is even lower. Given the 1-10% incidence of the complication of aseptic meningitis in spontaneous infections; as well as the risk of hearing loss, the need for extended absence from nursery or elementary school when infected; and the high incidence in children aged 3-6; it is recommended that children be vaccinated at the same time as, or as soon as possible after, MR vaccine phase 1, the first varicella vaccine injection, the Hib vaccine booster, and the pediatric pneumococcus vaccine booster, etc., and at the very latest, no later than 3 years of age, which is the high incidence age. To ensure the preventative effect, the Japan Pediatric Society recommends the second vaccination to be given at the same time as the MR vaccine phase 2.

Form 2

Vaccine Screening Questionnaire for [ ] (infant/schoolchild)

		Body temperature before interview			Degrees
Address					
Child's Name		M	Birth date	Born on / / (d/m/y)	
Parent/Guardian's Name		F		Age (years months)	

Questionnaire for Vaccination	Answer		Doctor's comment
Have you read the document (sent to you previously by the municipal office) explaining the vaccination that will be administered today?	Yes	No	
Please answer the following questions about the child. Birth Weight Did the child have any abnormal findings at delivery? ( ) g Did the child have any abnormal findings after birth? Was any abnormality identified at an infant health check?	Yes Yes Yes	No No No	
Is the child sick today? If so, describe the nature of the illness. ( )	Yes	No	
Has the child been ill in the past month? Disease name ( )	Yes	No	
Has any family member or friend of the child had measles, rubella, chickenpox or mumps in the past month? Disease name ( )	Yes	No	
Has the child been exposed to anyone with tuberculosis (including family members)?	Yes	No	
Has the child been vaccinated in the past month? Vaccine name ( )	Yes	No	
Does the child have a congenital anomaly, heart, kidney, liver, central nerve disease, immune deficiency, or any other diseases for which you have consulted a doctor? Disease name ( )	Yes	No	
Where relevant, did the doctor who manages the above disease agree with today's vaccination?	Yes	No	
Has the child had a seizure (spasm or fit) in the past? If so, at what age did it occur? ( )	Yes	No	
If you answered "yes" to the preceding question, did the child have a fever at that time?	Yes	No	
Has the child ever had a rash or urticaria (hives or 'nettle rash') as a reaction to medications or food or become ill after eating certain foods or receiving certain medications?	Yes	No	
Does the child have a family member or relative with a congenital immunodeficiency?	Yes	No	
Has the child had a serious reaction to a vaccine in the past? Vaccine name ( )	Yes	No	
Has any family member or relative of the child had a serious reaction to a vaccine in the past?	Yes	No	
Has the child received a transfusion of blood or blood products or been given a medicine called gamma globulin in the past 6 months?	Yes	No	
Do you have any questions about today's vaccination?	Yes	No	
Doctor's comment Based on the above answers and the results of interview, I have decided that the child (can / should not) receive a vaccination today. I have explained to the parent/guardian the information concerning the benefits and side effects of vaccination and the support provided to people who have had adverse events associated with vaccination. Signature or Name and Seal of Doctor:			

This screening questionnaire is used to improve the safety of vaccination. The child has been interviewed by the doctor, and information concerning the benefits, objectives, and risks (including serious side effects) of vaccination has been explained to me by the doctor, as has the nature of support provided if adverse events occur. I believe that I understand this information.
I (do / do not)* give consent for the child to be vaccinated. * Please circle your choice.
I understand the above and agree that this questionnaire can be submitted to the municipal office.
Signature of Parent / Guardian:

Vaccine Name	Dosage	Institution / Doctor Name / Date Administered
Vaccine Name Lot Number [Caution] Confirm that the expiration date of the vaccine is valid.	* Vaccination method mL	Institution: Doctor Name: Date Administered: / / (d/m/y)

[Note] Gamma globulin is a blood product that is injected to prevent infections, such as type A hepatitis, and to treat severe infections. Certain vaccines (for example, measles vaccine) are occasionally less effective in people who have received this product in the preceding 3 to 6 months.

* For BCG vaccination, enter "percutaneous injection at the prescribed dose using an apparatus with multiple needles for BCG" etc., and for 5-type combination vaccine or pneumococcal 15-valent conjugate vaccine, enter "subcutaneous or intramuscular injections", respectively.

Form 8

Hepatitis B Vaccine Screening Questionnaire

		Body temperature before interview			Degrees
Address					
Child's Name		M F	Birth date	Born on / / (d/m/y) Age (years months)	
Parent/Guardian's Name					

Questionnaire for Vaccination	Answer		Doctor's comment
Have you read the document (sent to you previously by the municipal office) explaining the vaccination that will be administered today?	Yes	No	
Please answer the following questions about the child. Birth Weight ( ) g Did the child have any abnormal findings at delivery? Did the child have any abnormal findings after birth? Was any abnormality identified at an infant health check?	Yes Yes Yes	No No No	
Is the child sick today? If so, describe the nature of the illness. ( )	Yes	No	
Has the child been ill in the past month? Disease name ( )	Yes	No	
Has any family member or friend of the child had measles, rubella, chickenpox or mumps in the past month? Disease name ( )	Yes	No	
Has the child been vaccinated in the past month? Vaccine name ( )	Yes	No	
Does the child have a congenital anomaly, heart, kidney, liver, central nerve disease, immune deficiency, or any other diseases for which you have consulted a doctor? Disease name ( )	Yes	No	
Where relevant, did the doctor who manages the above disease agree with today's vaccination?	Yes	No	
Has the child had a seizure (spasm or fit) in the past? If so, at what age did it occur? ( )	Yes	No	
If you answered "yes" to the preceding question, did the child have a fever at that time?	Yes	No	
Has the child ever had a rash or urticaria (hives or 'nettle rash') as a reaction to medications or food or become ill after eating certain foods or receiving certain medications?	Yes	No	
Does the child have a family member or relative with a congenital immunodeficiency?	Yes	No	
Has the child had a serious reaction to a vaccine in the past? Vaccine name ( )	Yes	No	
Has any family member or relative of the child had a serious reaction to a vaccine in the past?	Yes	No	
Has the child received a transfusion of blood or blood products or been given a medicine called gamma globulin in the past 6 months?	Yes	No	
Did the child receive the hepatitis B vaccine after birth as part of the mother-to-infant transmission prevention program?	Yes	No	
Do you have any questions about today's vaccination?	Yes	No	
Doctor's comment Based on the above answers and the results of interview, I have decided that the child (can / should not) receive a vaccination today. I have explained to the parent/guardian the information concerning the benefits and side effects of vaccination and the support provided to people who have had adverse events associated with vaccination. Signature or Name and Seal of Doctor:			

This screening questionnaire is used to improve the safety of vaccination. The child has been interviewed by the doctor, and information concerning the benefits, objectives, and risks (including serious side effects) of vaccination has been explained to me by the doctor, as has the nature of support provided if adverse events occur. I believe that I understand this information.
I (do / do not)* give consent for the child to be vaccinated. * Please circle your choice.
I understand the above and agree that this questionnaire can be submitted to the municipal office.
Signature of Parent / Guardian:

Vaccine Name	Dosage	Institution / Doctor Name / Date Administered
Vaccine Name Lot Number [Caution] Confirm that the expiration date of the vaccine is valid.	* (Subcutaneous injection) mL	Institution: Doctor Name: Date Administered: / / (d/m/y)

Form 10

Rotavirus Vaccine Screening Questionnaire

Parent/guardian: Please fill out the bolded fields.

			Date	/ / (YYYY/MM/DD)
Address			**Pre-exam temperature**	degrees (include decimal)
			Phone no.	– –
Child's name		**M / F**	**Child's date of birth**	/ / (YYYY/MM/DD)
Parent/guardian's name				(Age: weeks days) For age in weeks and days, count the day after the date of birth as day 1.

If this is the first vaccination, have you confirmed that the child is not older than 14 weeks and 6 days as of today?	Field for medical institution to enter (Mark a ☑)

Questionnaire	Answer			Doctor's comment
Which vaccination will your child receive today?	1st	2nd	3rd	
Please write the date(s) of the vaccination(s) your child has received so far (answer only if this is your child's 2nd or 3rd vaccination). Note: Confirm that at least 27 days have passed since your child's last rotavirus vaccination.	1st / / (YYYY/MM/DD) 2nd / / (YYYY/MM/DD)			
Have you read the document provided by the municipal office explaining the vaccination that will be administered today?	Yes	No		
Do you understand the benefits and side effects of the vaccination that will be administered today?	Yes	No		
Were you provided with information concerning intussusception, and did you understand that information?	Yes	No		
The following questions concern your child's growth and development. Birth weight:	g			
Were there any abnormalities at the time of delivery?	Yes	No		
Have there been any abnormalities after birth?	Yes	No		
Have any abnormalities been identified in an infant health exam?	Yes	No		
Is your child experiencing any illness or does your child feel unwell today? Please describe the symptoms:	Yes	No		
Has your child been sick within the last month? Name of illness:	Yes	No		
Has any family member or friend of the child had measles, rubella, chickenpox, or mumps in the past month? Name of illness:	Yes	No		
Has your child been vaccinated within the past month? Vaccine: Date: (YYYY/MM/DD)	Yes	No		
Has your child experienced intussusception before? Or does your child have an untreated congenital abnormality of the gastrointestinal tract? Note: If yes, your child cannot receive the rotavirus vaccine.	Yes	No		
Has your child been diagnosed with immunodeficiency? Or has your child experienced repeated diarrhea, repeated infections such as pneumonia or middle ear infections, or had difficulty gaining weight? Note: If yes, your child may not be able to receive the rotavirus vaccine.	Yes	No		
Does your child have a congenital anomaly; gastrointestinal disorder; heart, kidney, liver, blood, or central nervous disease; or any other diseases for which you have consulted a doctor? Name of illness:	Yes	No		
If you answered yes to the previous question, have you been told by the doctor whom your child is seeing for that disease that your child may receive today's vaccination?	Yes	No		
Has your child had a seizure (spasm or fit) in the past? If so, at around how many months of age: months	Yes	No		
If you answered yes to the previous question, did your child have a fever at that time?	Yes	No		
Has your child ever had a rash or hives or become ill after eating certain foods or receiving certain medications?	Yes	No		
If you answered yes to the previous question, name of medication/food:				
To date, has your child ever felt ill after receiving a vaccination?	Yes	No		
If you answered yes to the previous question, name of vaccine:				
Did the mother take medication which suppresses the immune system while pregnant with the child?	Yes	No		
If you answered yes to the previous question, name of medication:				
Has a close relative of your child been diagnosed with a congenital immunodeficiency?	Yes	No		
Has a close relative of your child ever felt ill after receiving a vaccination?	Yes	No		
To date, has your child received a blood transfusion or been injected with gamma globulin?	Yes	No		
Do you have any questions about today's vaccination?	Yes	No		

Field for doctor to enter

Based on the above questionnaire and the results of the medical examination, I have decided that the child **(can / should not)** receive today's vaccination.
I have explained to the parent/guardian the information concerning the benefits and side effects of vaccination (particularly intussusception) and the Relief System for Injury to Health with Vaccination.

Signature or name and seal of doctor:

Field for parent/guardian to enter

My child has been examined by and I have been provided with information by the doctor. I understand the benefits, objectives, possibility of serious side effects (particularly intussusception), and information concerning the Relief System for Injury to Health with Vaccination, and accordingly I **(do / do not)*** give consent for my child to be vaccinated. * Please circle your choice.
I understand that the purpose of the questionnaire is to ensure the safety of vaccinations and I agree that this questionnaire can be submitted to the municipal office.

Signature of parent/guardian:

Vaccine used	**Dosage**		**Place of vaccination/doctor's name/date of vaccination**
Vaccine name:	**Oral vaccination**		Place of vaccination:
Lot no.:	RotaTeq® 2 ml	Rotarix® 1.5 ml	Doctor's name:
Warning: Confirm that expiration date of vaccine is valid			Date of vaccination: / / (YYYY/MM/DD)

[Reference 4] Post-vaccination health survey

This table summarizes the incidence of fever and local reactions based on the Ministry of Health, Labour and Welfare 2021 post-vaccination health survey summary report. It also summarizes the values of the relatively possible typical symptoms of BCG, seasonal influenza, and, pneumococcus in the elderly. This table includes both single and simultaneous vaccinations. Since there are many types of vaccines given between the ages of 0 and 1, they are often given simultaneously. Please refer to the report for the health condition after simultaneous vaccination.

2021 Survey on Health Status after Vaccination

Vaccine type*	Number of people surveyed	All cases of fever (%)	37.5˚C to 38.4˚C (%)	38.5˚C or higher (%)	Local reaction (%)
DPT-IPV phase 1 1st dose (primary)	1,327	14.8	9.9	4.8	8.4
DPT-IPV phase 1 2nd dose (primary)	991	14.6	10.2	4.4	12.2
DPT-IPV phase 1 3rd dose (primary)	1,065	2.8	1.9	0.9	6.4
DPT-IPV phase 1 booster	972	10.4	6.2	4.2	7.5
DT phase 2	1,549	1.9	1.4	0.5	24.9
MR phase 1	1,759	13.2	6.0	7.2	5.8
MR phase 2	1,332	2.9	1.4	1.5	2.9
Japanese encephalitis phase 1 1st dose (primary)	1,278	14.8	7.1	7.7	2.7
Japanese encephalitis phase 1 2nd dose (primary)	805	6.0	3.1	2.9	2.4
Japanese encephalitis phase 1 booster	728	6.0	3.6	2.5	2.9
Japanese encephalitis phase 2	366	2.2	1.6	0.5	6.3
Hib phase 1 1st vaccination	1,177	4.2	3.4	0.8	4.2
Hib phase 1 2nd vaccination	1,037	16.7	11.2	5.5	11.2
Hib phase 1 3rd vaccination	992	12.9	9.1	3.8	11.5
Hib booster	786	17.8	8.0	9.8	7.9
Pediatric pneumococcus phase 1 1st vaccination	1,287	5.5	3.8	1.7	12.5
Pediatric pneumococcus phase 1 2nd vaccination	1,168	14.6	9.7	4.9	16.7
Pediatric pneumococcus phase 1 3rd vaccination	1,051	12.1	8.9	3.1	16.6
Pediatric pneumococcus booster	816	21.7	11.4	10.3	22.1
Varicella 1st vaccination	1,536	16.1	6.2	10.0	4.5
Varicella 2nd vaccination	1,374	10.3	4.3	6.0	3.4
Hepatitis B 1st dose (primary)	1,430	4.8	4.3	0.6	4.1
Hepatitis B 2nd dose (primary)	1,248	13.9	9.0	4.9	9.9
Hepatitis B 3rd dose (primary)	1,125	5.1	2.3	2.8	7.7

Vaccine type*	Number of people surveyed	All cases of fever (%)	37.5˚C to 38.4˚C (%)	38.5˚C or higher (%)	Diarrhea (%)
Rotavirus phase 1 1st vaccination	1,721	4.9	3.7	1.3	2.7
Rotavirus phase 1 2nd vaccination	1,324	12.8	8.2	4.7	3.0
Rotavirus phase 1 3rd vaccination	267	15.4	12.0	3.4	3.0

*Includes the incidence of all cases of fever and local reactions during the survey period (28 days).

The table below shows the incidence of "lymphadenopathy" and "local skin moisturization" selected as relatively possible typical symptoms of BCG, as well as the "total incidence of all symptoms." Only the BCG survey period is 4 months.

Vaccine type	Number of people surveyed	Lymphadenopathy (%)	Local skin moisturization (%)	Total incidence of all symptoms (%)
BCG	1,622	0.4	0.0	0.4

References (for details, see: https://www.yoboseshu-rc.com/publics/index/7)

1 Vaccination Guidelines

March 2024 revised edition (A5 size)

A guidebook on medical and regulatory information about vaccination for medical staff in practice to conduct safe and appropriate vaccination.

2 "Influenza and Pneumococcal Disease (Category B Disease) Vaccination Guidelines"

2023 edition (A5 size)

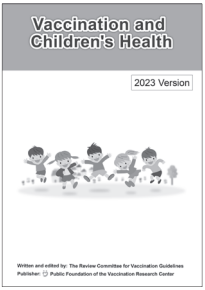
An overview of medical and regulatory information on influenza vaccination and routine vaccination of the elderly for pneumococcal disease.

3 Vaccination handbook

2023 edition (A4 size)

A handbook for doctors who give vaccination and municipal staff in charge of vaccination.

4. Editions in foreign languages "Vaccination and children's health"



March 2023 revised edition

"Vaccination and children's health," a brochure containing correct knowledge and information concerning vaccination for parents and the vaccination screening questionnaire, is translated in the following languages and available from the following site. Please download them as required.

https://www.yoboseshu-rc.com/publics/index/8/

The entire brochure is available in the following 10 languages: English, Chinese, Korean, Vietnamese, Spanish, Portuguese, Thai, Indonesian, Tagalog, and Nepalese
The vaccination questionnaire alone is available in the following seven languages: Arabic, Italian, German, French, Mongolian, Russian, and Ukranian.

5 Learn about vaccinations with your children

August 2023 edition (A5 size)

With a comic aimed at children and guidance aimed at adults, this one book will allow you to better understand vaccinations.

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