Immunization

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Abstract

Immunization has played a major role in protection against infectious disease, and indeed the development of vaccines has been classed as one of the greatest medical achievements. The introduction of vaccines has been so successful that we are on the verge of seeing the eradication of several vaccine-preventable diseases. Moreover, the proportion of disease prevented by the routine childhood immunization schedule is higher than for any other routine public health intervention. To ensure the continued efforts of controlling, eliminating and eradicating infectious diseases, it is necessary to encourage the collaboration of health groups, organizations and the public to maintain adequate vaccine coverage and continue the development of effective and safe vaccines.

Keywords Immunization; infectious diseases; vaccine

Key points

- Vaccination is an effective and safe method of preventing serious infectious diseases
- Maintaining high vaccine coverage is crucial in preventing the re-emergence of disease
- Live vaccines are contraindicated in individuals who are immunosuppressed
- Childhood vaccinations should be given in a timely manner to all infants, especially premature infants
- Nucleic acid (RNA based) and viral-vectored vaccines have recently emerged as effective platforms for emerging infectious diseases

Introduction

Immunization is the process whereby individuals are made immune to infectious diseases. This can be achieved via active immunity, where immunity is induced by vaccination — the administration of antigens to the individual — or via passive immunity, where immunity is induced by the administration of antibodies to the individual.

Active immunity

Active immunity acquired through vaccination induces humoral and/or cell-mediated immune responses to provide protection, often similar to that derived from natural infection. Immunity generated by this mechanism is often long-lasting. Various types of vaccine are available: live attenuated, inactivated whole-cell (killed antigen), toxoid (inactivated toxins), subunit (purified antigen) and the newer nucleic acid (RNA, DNA) and viral vector vaccines.

Vaccination with *live attenuated vaccines* — for example, measles/mumps/rubella (MMR), rotavirus, smallpox, varicella-zoster, yellow fever, influenza, typhoid, tuberculosis (TB; bacillus Calmette–Guérin (BCG)), oral polio vaccine (OPV) — involves replication of the live attenuated organism in the host to give rise to an immune response that mimics that induced by natural infection. These vaccines confer long-lasting antibody responses after one or two doses and, because they are attenuated, they can cause subclinical infection, albeit with a very low risk of disease.

Inactivated vaccines can be made of whole, inactivated microorganisms (e.g. hepatitis A, Japanese encephalitis, rabies, inactivated polio vaccine (IPV)), or specific microbial components (toxoid and subunit vaccines). These vaccines cannot cause the disease that they are designed to protect against; however, they may not provide such long-term immunity as live attenuated vaccines, and multiple doses often need to be administered.

Toxoid vaccines (e.g. diphtheria, tetanus) are protein toxins that have been modified to reduce pathogenicity but are immunogenic. Other component vaccines are made from *purified subunits* (e.g. acellular pertussis, pneumococcus, meningococcus), engineered subunits (e.g. *Haemophilus influenzae* type B (Hib), pneumococcal and meningococcal polysaccharide conjugate vaccines) or recombinant subunits (hepatitis B, human papillomavirus (HPV)) of microorganisms that can induce immunity.

Newer types of vaccine include nucleic acid vaccines (RNA, DNA) and viral vectored vaccines (currently adenovirus vectors), which have been of particular value in the rapid development of effective vaccines against coronavirus disease 2019 (COVID-19).

Passive immunity

Passive immunization allows short-term protection from disease through the transfer of antibodies. This process occurs naturally during pregnancy, when immunoglobulin (Ig) G is transferred across the placenta to the fetus. Protection through passive immunization can also be conferred by the transfusion of blood or blood products including IgG (e.g. hepatitis B, tetanus, rabies, varicella-zoster) or by monoclonal antibodies (e.g. respiratory syncytial virus (RSV)). This mechanism can provide immediate, albeit short-lived protection.

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Vaccine failure

A small proportion of individuals are prone to infection despite vaccination. Vaccine failures can be categorized into primary and secondary. Individuals with primary vaccine failures do not have any immunological response to the vaccine. In those with secondary vaccine failure, there is an initial immunological response but this wanes over time. Booster doses can be required to prevent vaccine failure.

Herd immunity

Vaccines protect individuals directly and, by reducing the risk of transmission, can also lead to the protection of unvaccinated individuals as they are no longer being exposed to the infection. Herd immunity refers to the susceptible unvaccinated population being protected by the vaccinated population. It is, however, paramount that a high vaccine coverage is maintained to induce high levels of herd immunity and prevent the re-emergence of disease.

Vaccines (Table 1)

Diphtheria is caused by the action of diphtheria toxin, which is produced by *Corynebacterium diphtheriae* or *Corynebacterium ulcerans* and can result in paralysis and cardiac failure. The vaccine is made from a cell-free purified toxin treated with formaldehyde, converting it into diphtheria toxoid, and adsorbed onto an adjuvant.

Diphtheria vaccines are produced in two strengths: high dose (D), used in the primary immunization of children <10 years of age, and low dose (d), used in those aged ≥10 years, as well as for boosting. The vaccine is administered in a combined vaccine, and a total of six doses of diphtheria vaccine are given in the routine immunization schedule.

Tetanus is caused by the action of tetanus toxin, produced by the bacterium *Clostridium tetani* and resulting in generalized spasms and rigidity. The vaccine is made from a cell-free purified toxin treated with formaldehyde, converting it into tetanus toxoid, and is adsorbed onto an adjuvant.

The tetanus vaccine (T) is administered as part of a combined vaccine and is given as a six-dose regimen, as well as to individuals with tetanus-prone wounds. Tetanus immunoglobulin is also available for people at particularly high risk of disease.

Pertussis is a highly infectious disease caused by *Bordetella pertussis*. The vaccines are made from purified components of the *B. pertussis* organism and then adsorbed onto adjuvants.

The acellular pertussis vaccine is currently used in the UK primary immunization schedule and is given as part of a combined vaccine that is administered three times during the primary immunization schedule with a booster dose at 18 months and 3 years of age. The incidence of local and systemic reactions is lower with the acellular pertussis (aP) vaccine compared with the previously used whole-cell pertussis vaccine.

In response to the pertussis outbreak in 2012, the UK Department of Health introduced a programme offering pertussis vaccination to pregnant women between 28 and 32 weeks of pregnancy. This was put in place to protect infants, from birth, by passive immunity until they were old enough to be protected through routine immunization. The minimum gestational age for vaccination was subsequently reduced to 16 weeks.

Poliomyelitis is caused by one of three serotypes of poliovirus (serotypes 1, 2 and 3). Until 2004, the live attenuated OPV (Sabin) was used for routine immunization in the UK. Because of the risk of vaccine-associated paralytic polio with OPV, it was replaced by IPV as part of a combined vaccine.

A regimen of six doses of IPV (four doses in the routine primary immunization schedule with a booster dose at 3 years and at 14 years of age) provides long-term protection.

***Haemophilus influenzae* type b** can cause serious invasive disease, especially meningitis. The Hib vaccine is a protein–polysaccharide conjugate vaccine. In the UK, it is available as part of the combined 6-in-1 vaccine (Infanrix hexa – DTaP/IPV/Hib/hepatitis B) given in three doses before 1 year of age.

In 2026, a fourth dose of Infanrix hexa will be introduced as part of a new routine vaccination appointment at 18 months of age. This change follows the discontinuation of the combined Hib/MenC (meningococcal C) vaccine previously given at 12 months, prompting its replacement with the 18-month hexavalent dose.

Hepatitis B vaccine is produced using recombinant DNA technology and adsorbed onto an adjuvant. The regimen involves doses of hepatitis B vaccine at birth and at 1 month of age for individuals at high risk of exposure (Table 2). A specific hepatitis B immunoglobulin is also available to provide passive and temporary immunity in individuals exposed to the virus.

The hexavalent combination vaccine Infanrix hexa (DTaP/IPV/Hib/hepatitis B) was introduced in 2017 in place of the 5-in-1 vaccine (DTaP/IPV+Hib) for primary immunization, adding protection against hepatitis B. The new 18-month vaccination appointment includes a sixth dose of hepatitis B, delivered as part of the hexavalent vaccine. This replaces the previously given monovalent hepatitis B dose at 12 months.

Hepatitis A vaccines can be given to high-risk individuals as a monovalent vaccine (whole, inactivated virus) or combined with either a typhoid or hepatitis B vaccine. Human normal immunoglobulin can be used to provide immediate but temporary immunity.

Pneumococcal vaccines are available as pneumococcal polysaccharide vaccine (PPV) and pneumococcal conjugate vaccines (PCV). PPV contains purified capsular polysaccharide from 23 capsular types of pneumococcus, with eight of the 10 most prevalent serotypes causing invasive pneumococcal disease included. PPV is used in individuals aged ≥65 years and in at-risk patients aged ≥2 years.

PCV contains polysaccharide from common capsular types and is conjugated to proteins (PCV7, PCV10, PCV13), which improves its immunogenicity. Unlike PPV, this conjugate vaccine confers immunity in infants from 2 months of age. Currently, in the UK immunization schedule, PCV13 is given as a two-dose regimen, with one dose at 16 weeks and the other at 1 year of age.

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Recommended schedule for the UK's routine immunizations

Age due	Disease	Vaccine	How it is given
2 months	Diphtheria, tetanus, pertussis, polio and *Haemophilus influenzae* serotype b and hepatitis B	DTaP/IPV/Hib/HepB	One injection
	Meningococcal group B	MenB	One injection
	Rotavirus	Rotavirus	One oral application
3 months	Diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* serotype b and hepatitis B	DTaP/IPV/Hib/HepB	One injection
	Meningococcal group B	MenB	One injection
	Rotavirus	Rotavirus	One oral application
4 months	Diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* serotype b and hepatitis B	DTaP/IPV/Hib/HepB	One injection
	Pneumococcal (13 serotypes)	PCV	One injection
12 months	[a]Measles, mumps, rubella, varicella	MMRV	One injection
	Pneumococcal (13 serotypes)	PCV	One injection
	Meningococcal group B	MenB	One injection
18 months	[a]Diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* serotype b and hepatitis B	DTaP/IPV/Hib/HepB	One injection
	[a]Measles, mumps, rubella, varicella	MMRV	One injection
2 years to <18 years	Influenza (annually)	LAIV	Nasal spray (if LAIV is contraindicated and child is in a clinical risk group, give inactivated influenza vaccine)
3 years and 4 months	Diphtheria, tetanus, pertussis, polio	dTaP/IPV	One injection
12–13 years	Cervical cancer caused by HPV types 6, 11, 16 and 18	HPV	One injection
14 years	Tetanus, diphtheria and polio	Td/IPV	One injection
	Meningococcal groups ACWY	MenACWY	One injection
65 years	Pneumococcal (23 serotypes)	PPV	One injection
	Influenza (annually)	Inactivated influenza vaccine	One injection
	Shingles	Shingles	One injection
70 years (and severely immunocompromised individuals ≥18 years)	Shingles	Shingles	One injection
75 years	RSV	RSV	One injection

Recommended schedule for the UK's routine immunizations. Adapted from UK Health Security Agency, UK.[1]
For abbreviations, see text.
[a] Implementation from 2026.

Table 1

Rotavirus vaccine was introduced into the UK immunization schedule in 2013 to protect babies and infants from this cause of diarrhoea and vomiting. It is a live attenuated vaccine given orally at 2 months and 3 months of age.

Meningococcal disease is caused by *Neisseria meningitidis*. 12 capsular groups have been identified, groups B, C, W and Y being the most common. There have been a number of changes to the meningococcal UK vaccination schedule that reflect the epidemiological changes in capsular groups causing invasive meningococcal disease over time.

Infant doses of the MenC vaccine were removed from the UK schedule in 2016 because of the low incidence of meningococcal C disease in this age group, leaving a single combined Hib/MenC (Menitorix) dose at 12 months. From 2025, this 12-month dose was no longer offered, after the discontinuation of Menitorix and the continued success of the adolescent MenACWY programme in controlling MenC disease. Because of an increase in meningococcal capsular group W (MenW) disease, a change from the adolescent MenC vaccine to the quadrivalent ACWY conjugate vaccine was made.

In 2015, a meningococcal group B (MenB) vaccine was added to the routine UK immunization schedule to provide protection against infection caused by meningococcal group B strains. Because of a shift in the peak age of MenB infection from 5–6 months to 1–3 months, the previous vaccination schedule of

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Selective immunization programme

Target group	Age and schedule	Vaccine
Babies born to hepatitis B-infected mothers	At birth, 1 month	Hepatitis B
Infants in areas of the country with an incidence of TB ≥40/100,000	At approximately 28 days	BCG
Infants with a parent or grandparent born in a high-incidence country	At approximately 28 days	BCG
Pregnant women	During influenza season at any stage of pregnancy	Influenza
	From 16 weeks' gestation	Pertussis
	From 28 weeks' gestation	RSV

Selective immunization programme. Adapted from UK Health Security Agency, UK.[1]

Table 2

2, 4, and 12 months has been updated to a 2, 3 and 12-month schedule to provide earlier protection.

MMR vaccines consist of live attenuated strains of measles, mumps and rubella viruses. This vaccine is given to children as a two-dose regimen, with the first dose at 12–13 months of age. Previously given at 3 years of age, the second dose of the MMR vaccine will, from 2026, be offered at 18 months under the revised immunization schedule. This change aims to improve coverage and provide earlier protection against measles, mumps and rubella, helping to reduce the risk of outbreaks.

Influenza vaccines (inactivated influenza vaccine) are prepared each year in line with the circulating strains recommended by the World Health Organization. In the UK, the vaccination is currently offered annually to individuals aged ≥50 years who have underlying health conditions, those who are pregnant or in long-stay residential care, and carers and frontline health or social care workers.

In 2012, the influenza vaccine programme was extended to all children aged 2 to <18 years of age using the intranasal live attenuated influenza vaccine (LAIV). LAIV has been shown to provide a high level of protection for children, with an efficacy against disease of 83%.[2]

Varicella (chickenpox) is an acute, highly infectious disease caused by varicella-zoster virus. Herpes zoster (shingles) is caused by the reactivation of varicella virus. The varicella vaccine is a live attenuated virus given as two doses. This schedule provides about 98% protection in children[3] and will be introduced in the UK as a combined measles, mumps, rubella, and varicella (MMRV) vaccine at 12 and 18 months of age.

The shingles vaccine is routinely offered to adults from 65 years of age. Human varicella-zoster immunoglobulin can be given after exposure to chickenpox or herpes zoster (post-exposure prophylaxis) in patients unable to receive oral antivirals.

TB is caused by infection with the *Mycobacterium tuberculosis* complex (*M. tuberculosis*, *M. bovis*, *M. africanum*). The BCG vaccine contains live attenuated organisms. It must be given by intradermal injection, usually in the left upper arm. No further vaccinations should be administered in the same limb for at least 3 months because of the risk of lymphadenitis. A single dose of the BCG vaccine should be offered to individuals at increased risk of developing severe disease and/or of exposure to TB infection (Table 2).

HPV is a double-stranded DNA virus that infects squamous epithelia. HPV vaccines are subunit vaccines that mimic the virus without containing viral DNA. Since their introduction in 2008 they have been found to reduce abnormal screening tests, colposcopies and excisions. A two-dose regimen in girls aged 11–13 years was introduced in the UK in 2014, and was extended to adolescent boys in 2018. It is now offered as a one-dose schedule for boys and girls aged 12–13 years.

RSV is an RNA virus and a common cause of respiratory tract infections. To protect newborns, the UK introduced a maternal RSV vaccination programme in September 2024. Pregnant women are offered a single dose of Abrysvo vaccine, a bivalent recombinant protein vaccine targeting the prefusion F proteins of RSV subgroups A and B, from 28 weeks gestation. Clinical trials have demonstrated a significant reduction in the risk of severe RSV-related lower respiratory tract disease in infants in their first 6 months of life.

Nirsevimab, a long-acting monoclonal antibody, has been implemented in multiple countries for routine infant protection, administered as a single-dose during the RSV season. Some countries have adopted a dual strategy, offering maternal RSV vaccination in pregnancy alongside infant monoclonal antibody. In the UK nirsevimab is used selectively for very high-risk infants in addition to the maternal RSV vaccine programme. RSV vaccination is also recommended for adults aged ≥75 years in the UK.

COVID-19 vaccines have been rapidly developed using traditional techniques (inactivated virus, protein or peptide subunit vaccines) as well as novel platforms (nucleic acid and virus vector). Most vaccines are based on immunization with the spike protein, which is the main target for neutralizing antibodies. Two mRNA vaccines are currently used in the UK – Comirnaty and Spikevax.

The duration of immunity and how protective these updated vaccines will be to new and emerging variants of the virus remains to be determined. It is anticipated that annual booster campaigns will continue, focusing on high-risk groups.

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Immunization schedule in the UK

Tables 1–3 show the UK recommended routine immunization schedule, selective immunization programme and additional vaccines.[1]

Maternal immunizations

In the UK, pregnant women are currently offered vaccines to protect against pertussis, influenza and RSV (Table 2).

The pertussis vaccine was introduced in 2012 in response to an increased number of infant deaths from the disease. Prenatal pertussis vaccination provides passive immunity for the infant through intrauterine transfer of maternal antibodies. This intervention proved effective as, only 1 year after introducing this intervention, the estimated vaccine efficacy of pertussis immunization during pregnancy for preventing laboratory-confirmed pertussis disease was 91% for infants <3 months of age.[4]

Inactivated influenza vaccine is offered to pregnant women because of their increased risk of serious illness from influenza. Prenatal influenza vaccination also confers protection on infants in their first few months of life through passive immunity.

Since 2024, the UK has offered RSV vaccination to pregnant women from 28 weeks' gestation to provide passive protection to newborns in their early months of life. Pregnant women who are also immunosuppressed because of a health condition or treatment are considered at increased risk of COVID-19 and are offered the licensed COVID-19 vaccines.

Additional vaccines

Medical condition	Vaccine
Asplenia/splenic dysfunction	Meningococcal groups ABCWY
	Pneumococcal
	Influenza
Chronic heart and respiratory conditions	Pneumococcal
	Influenza
Chronic kidney disease	Pneumococcal
	Influenza
	Hepatitis B
Chronic liver conditions	Pneumococcal
	Influenza
	Hepatitis A
	Hepatitis B
Chronic neurological conditions	Pneumococcal
	Influenza
Cochlear implants	Pneumococcal
Complement disorders	Meningococcal groups ABCWY
	Pneumococcal
	Influenza
Diabetes mellitus	Pneumococcal
	Influenza
Haemophilia	Hepatitis A
	Hepatitis B
Immunosuppression caused by disease or treatment	Pneumococcal
	Shingles vaccine
	Influenza

Additional vaccines. Adapted from UK Health Security Agency, UK.[1]

Table 3

Contraindications

All vaccines are contraindicated in individuals with: (1) a confirmed anaphylactic reaction to a previous dose of the same vaccine; or (2) a confirmed anaphylactic reaction to a component that is contained in the vaccine. Live vaccines are also contraindicated in:

- severe primary or acquired immunodeficiency
- patients being treated for malignant or non-malignant disease with immunosuppressive chemotherapy or radiotherapy
- patients who have had a solid organ transplant and are on immunosuppressive treatment
- patients on immunosuppressive biological therapy
- patients being given systemic high-dose corticosteroids, until at least 3 months after completion of the corticosteroid treatment
- pregnant women.

Adverse events

Adverse events following immunization (AEFIs) can be categorized into one of four groups: programme-related, vaccine-induced, coincidental and unknown.

- **Programme-related** adverse events occur as a result of problems in providing and administering vaccines (e.g. wrong dose, expired vaccine, inappropriate route, site or technique of administration, incorrect vaccine preparation, incorrect vaccine reconstitution).
- **Vaccine-induced** adverse events are true reactions caused by a particular vaccine or a constituent of the vaccine (e.g. local reactions and fever within 48 hours of DTaP/IPV/Hib/HepB and MenB, rash and fever 7–10 days after MMR).
- **Coincidental** AEFIs are not true adverse reactions after immunization and are only associated with the vaccine because of the timing of their occurrence.
- **Unknown** AEFIs include reactions that do not fit into any of the other AEFI categories.

Common vaccine-induced AEFIs include pain, swelling/redness at the injection site and systemic adverse reactions (fever, malaise, myalgia, irritability, headache). These reactions do not contraindicate further doses of vaccine. Other rare vaccine-induced AEFIs include neurological or immune-mediated such as seizures, hypotonic-hyporesponsive episodes, idiopathic thrombocytopenic purpura, allergic reactions and anaphylaxis.

Management

Advice should be offered to parents regarding what AEFIs are expected and the use and dose of paracetamol or ibuprofen to prevent or treat a fever. Fevers are common and usually mild, and local reactions are usually self-limiting.

Anaphylactic reactions

These reactions are rare and occur at a rate of approximately 1 per million administered doses. The onset is typically rapid, but

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the reaction generally responds to parenteral adrenaline (epinephrine). It is essential that all health professionals involved in immunization are familiar with resuscitating individuals with anaphylactic reactions.

Special considerations

Many individuals have medical conditions that put them at increased risk of complications from infectious diseases. It is important that these individuals are fully immunized with routine and additional vaccinations as well as additional doses to provide adequate protection (Table 3).

Prematurity

All vaccines in the routine immunization schedule should be given to premature infants at the appropriate chronological age according to the schedule used for full-term infants regardless of birthweight. Premature infants are adequately protected by the current available vaccines when they are given using the same schedule as that used for full-term infants.

Although studies show that an impaired immune response may be seen in premature infants, resulting in reduced antibody production and cell-mediated immunity, antibody production is usually high enough to provide short-term protection. Furthermore, there is usually a good immune response after booster doses, indicating that normal immune memory is established.[5] In addition, the safety and tolerability of all the recommended vaccines given to premature infants are no different from those for full-term infants.

Future vaccine developments

As immunization plays a crucial role in our efforts to eradicate vaccine-preventable diseases it is essential to continue the work of developing effective and safe vaccines. Examples of continuing vaccine research include:

- novel antigen delivery systems and adjuvants to enhance humoral and cellular immune responses for vaccines
- new vaccines for maternal immunization to protect newborn infants from infectious diseases (e.g. group B *Streptococcus*)
- new vaccine delivery methods, for example orally, or topically via vaccine patches
- new or improved vaccines against important diseases such as norovirus, Zika virus, cytomegalovirus, group A *Streptococcus*, herpes simplex virus and TB. ◆

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FURTHER READING

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online here.

Question 1

An 8-week-old baby, born at 32 weeks' gestation, had been recently discharged from hospital and had presented for his first 2-month routine immunizations.

What is the appropriate approach to this?

A. He is eligible and should be given all routine 2-month vaccines as usual
B. He is not eligible because his age should be 'corrected' for his prematurity so he is too young
C. He is eligible for the routine vaccines but should not be given the rotavirus vaccine as this is a live vaccine
D. He is eligible for the routine vaccines and additionally should be given the influenza vaccine (in season)
E. He is eligible but should be given the vaccines under observation in hospital as he may be more likely to have adverse effects

Question 2

A 3-year-old girl is being treated for acute lymphoblastic leukaemia (ALL). She is afebrile and clinically stable at a routine clinic visit during the winter season.

Which is the best strategy to reduce her risk of vaccine-preventable infection at home?

A Give the measles/mumps/rubella (MMR) vaccine now because she is afebrile
B. Defer all vaccines until her chemotherapy is complete
C. Her younger brother may be offered the chickenpox vaccine if he has not had chickenpox
D. As soon as she has finished her ALL treatment she should have a booster dose of all the routine vaccines
E. Give the bacillus Calmette–Guérin (BCG) vaccine now due to her increased infection risk

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Question 3

A healthy pregnant women is currently at 20 weeks of gestation and has a number of questions about vaccines.

Which of these is the most accurate statement?

A. She does not need to have a pertussis-containing vaccine if she has had one in the last 10 years
B. The only value of the influenza vaccine is to protect her against influenza
C. The respiratory syncytial virus (RSV) vaccine should only be offered if she has had another child who had severe RSV infection
D. If the pertussis vaccine is given within 1 week of delivering her baby it may not offer full protection to the baby
E. She should not be given the RSV vaccine if she has previously had a baby that was born prematurely

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