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Contraindications and special considerations

Almost all individuals can be safely vaccinated with all vaccines. In very few individuals, vaccination is contraindicated or should be deferred. Where there is doubt, rather than withholding vaccine, advice should be sought from an appropriate specialist.

Vaccination providers should consider whether to avoid specific vaccinations in the following:

- individuals with a history of a confirmed anaphylactic reaction to a previous dose of the vaccine
- individuals with a history of a confirmed anaphylactic reaction to a component of the vaccine
- individuals with primary or acquired immunodeficiency
- individuals on current or recent immunosuppressive or immunosuppressive biological therapy
- infants born to a mother who received immunosuppressive biological therapy during pregnancy
- those in contact with an individual with immunodeficiency, current recent immunosuppressive including biological therapy
- pregnant women

While certain vaccines may be contraindicated in individuals falling into one of the categories mentioned above, this is not automatically the case. In some instances, the benefit of that vaccination may outweigh the risk. In other instances, vaccination should be delayed rather than withheld, or alternative measures considered (see Chapter 7). Further detail is outlined below and in the disease-specific chapters.

Previous anaphylaxis to a vaccine or to a vaccine component

Confirmed anaphylaxis post-vaccination occurs extremely rarely. Data from the UK, Canada and the US point to rates of 0.65 to 3 anaphylaxis events per million doses of vaccine given (McNeil MM et al. 2015; Bohlke et al., 2003).

Individuals who have had confirmed anaphylactic reaction to a previous dose of a vaccine containing the same antigens, or a confirmed anaphylactic reaction to another component contained in the relevant vaccine should not receive the vaccine concerned. Other vaccines can and should be given where appropriate. Facilities for treating anaphylaxis should be available in all vaccination settings.

The most common allergens and vaccines known to contain them are listed below and discussed further in the appropriate chapters. The list is not exhaustive and anaphylactic reactions to other vaccine components are possible; if so, it may be necessary to check the summary of product characteristics and/or with the manufacturer to understand whether a specific vaccine contains the implicated component.

Egg allergy

- Influenza (see chapter 19)
- Tick-borne encephalitis (Chapter 31)
- Yellow fever (Chapter 35)
- Hepatitis A (Chapter 17)

Note: Recent data suggest that anaphylactic reactions to MMR vaccine are not associated with hypersensitivity to egg antigens. All children with egg allergy should receive the MMR vaccination as a routine procedure in primary care. See Chapter 21 (Measles) for more details.

Neomycin, streptomycin or polymyxin B allergies

- Pertussis (Chapter 24)
- Polio (Chapter 26)
- Tetanus (Chapter 30)
- Shingles (Chapter 28a)
- Varicella (Chapter 34)
- Measles, Mumps and Rubella (Chapters 21, 23 and 28)

Gelatine allergy

- Shingles (Chapter 28a)
- Varicella (Chapter 34)
- Measles, Mumps and Rubella (Chapters 21, 23 and 28)

Severe latex allergy

Some pre-filled syringes may contain latex proteins in the tip cap and/or rubber plunger of the syringe. Similarly, the stoppers of some vaccines supplied in vials may contain latex proteins. The following vaccines use latex in their packaging in the UK (Oxford vaccine Group, 2015):

- one of the Hepatitis B vaccines (HBVaxPro)
- one of the MenC vaccines (Menjugate)
- MenB vaccine (Bexsero)

It is theoretically possible that latex protein from these tip caps, plungers or vial stoppers may cause allergic reactions when the vaccines are administered to latex-sensitive individuals. There is little evidence that such a risk exists and any such risk would be extremely small (Russell et al., 2004).

As a precaution, if an individual has a history of severe (i.e. anaphylactic) allergy to latex, vaccines supplied in vials or syringes that contain latex should not be administered, unless the benefit of vaccination outweighs the risk of an allergic reaction to the vaccine. Where possible, an alternative latex-free vaccine that covers the same disease should be administered. For latex allergies other than anaphylactic allergies (e.g. a history of contact allergy to latex gloves), vaccines supplied in vials or syringes that contain latex can be administered (ACIP, 2011).

Primary or acquired immunodeficiency

Live vaccines can, in some situations, cause severe or fatal infections in immunosuppressed individuals due to extensive replication of the vaccine strain. For this reason, individuals with some types of severe primary or acquired immunodeficiency (see list below) should not be given live vaccines, and vaccination in immunosuppressed individuals should only be conducted in consultation with an appropriate specialist. Inactivated vaccines cannot replicate and so may be administered to immunosuppressed individuals, although they may elicit a lower response than in immunocompetent individuals.

See Chapter 7: Immunisation of individuals with underlying medical conditions for further details.

Live vaccines currently available in the UK are:

- live influenza vaccine (Fluenz Tetra)
- Measles, Mumps and Rubella vaccine (Priorix, MMRVaxPro)
- Rotavirus vaccine (Rotarix)*
- Shingles vaccine (Zostavax)
- BCG vaccine
- Oral typhoid vaccine (Ty21a)
- Varicella vaccine (Varilrix, Varilvax)
- Yellow Fever vaccine

*Although the vaccine is a live attenuated virus, with the exception of severe combined immune-deficiency (SCID), the benefit from vaccination may exceed any risk in other forms of immunodeficiency

Most live vaccines should not be administered to individuals with primary or acquired immunodeficiency. This includes:

- immunosuppression due to acute and chronic leukaemias and lymphoma (including Hodgkin's lymphoma)
- severe immunosuppression due to HIV/AIDS (for BCG, the vaccine is contraindicated in all HIV positive individuals, see chapter 32)
- cellular immune deficiencies (e.g. Severe combined immunodeficiency, Wiskott-Aldrich syndrome, 22q11 deficiency/DiGeorge syndrome**)
- being under follow up for a chronic lymphoproliferative disorder including haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma and other plasma cell dyscrasias (list not exhaustive)

- having received an allogenic (cells from a donor) stem cell transplant in the past 24 months and only then if they are demonstrated not to have on-going immunosuppression or graft versus host disease (GVHD).
- having received an autologous (using their own stem cells) haematopoietic stem cell transplant in the past 24 months and only then if they are in remission

** Most patients with 22q11 deletion syndromes are able to receive live vaccines safely provided that they have no evidence of being severely immunocompromised (Perez et al.,2003). Specialist advice should always be sought to rule out severe immunosuppression.

Antibody deficiencies affecting IgG or IgA antibodies are not of themselves a contraindication to live vaccination unless associated with T cell deficiencies.

The 2013 Infectious Disease Society of America (IDSA) Clinical Practice Guideline for Vaccination of the Immunocompromised Host (see further resources) provides further detail for specific vaccines in specific conditions. If there is any doubt, immunological advice should be sought prior to administration. If healthcare professionals administering the vaccine have queries about a patient's degree of immunosuppression they should contact the relevant specialist for advice. In some situations, the specialist may make a decision that the risk of a specific disease outweighs any potential risk from the vaccine – the reasons for this should be clearly documented and this administration would generally require a patient specific direction.

Further detail about vaccines for specific diseases, including recommendations for HIV positive individuals, are listed in the appropriate chapters:

- Influenza vaccine (Chapter 19)
- Measles, Mumps and Rubella vaccine (Chapters 21, 23 and 28)
- Rotavirus vaccine (Chapter 27b)
- Shingles vaccine (Chapter 28a)
- BCG vaccine (Chapter 32)
- Oral typhoid vaccine (Chapter 33)
- Varicella vaccine (Chapter 34)
- Yellow fever (Chapter 35)

The British HIV association and the Children's HIV association (see further resources) provide further details on vaccination in HIV-positive individuals.

Immunosuppressive therapy (including biologics)

Individuals who are on or have recently received high doses of certain immunosuppressive or biological therapies (see list below) should not be given live vaccines because of the risk of severe or fatal infections. For those on lower doses of such therapies or those who completed therapy less recently live vaccination may go ahead after careful consideration. As the degree of attenuation, and the virulence of the infection, varies between live vaccines, it may be possible for some immunosuppressed individuals to receive some vaccines. Vaccination of immunosuppressed individuals should only be conducted in

consultation with an appropriate specialist. Inactivated vaccines cannot replicate and so may be administered to immunosuppressed individuals, although they may elicit a lower response than in immunocompetent individuals.

See Chapter 7: Immunisation of individuals with underlying medical conditions for further details.

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- live influenza vaccine (Fluenz Tetra)
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- BCG vaccine
- Oral typhoid vaccine (Ty21a)
- Varicella vaccine (Varilrix, Varilvax)
- Yellow Fever vaccine

Live vaccines should not be administered to individuals on immunosuppressive therapy including:

- those who are receiving, or have received in the past 6 months, immunosuppressive chemotherapy or radiotherapy for malignant disease or non-malignant disorders
- those who are receiving, or have received in the past 6 months, immunosuppressive therapy for a solid organ transplant (with exceptions, depending upon the type of transplant and the immune status of the patient)
- those who are receiving or have received in the past 12 months immunosuppressive biological therapy (e.g. anti-TNF therapy such as alemtuzumab, ofatumumab and rituximab) unless otherwise directed by a specialist
- those who are receiving or have received in the past 3 months immunosuppressive therapy including:
 - adults and children on high-dose corticosteroids (>40mg prednisolone per day or 2mg/kg/day in children under 20kg) for more than 1 week
 - adults and children on lower dose corticosteroids (>20mg prednisolone per day or 1mg/kg/day in children under 20kg) for more than 14 days
 - adults on non-biological oral immune modulating drugs e.g. methotrexate >25mg per week, azathioprine >3.0mg/kg/day or 6-mercaptopurine >1.5mg/kg/day
 - for children on non-biological oral immune modulating drugs (except those on low doses, see below), specialist advice should be sought prior to vaccination

As live vaccines replicate after administration, ideally individuals who have received a live vaccine should wait until their immune response has been established to receive immunosuppressive therapy. For most viral live vaccines a period of up to four weeks should be sufficient. However, as the vaccine viruses are generally attenuated, immunosuppressive treatment should not be delayed if this could result in worsening of the underlying condition. In such situations, additional measures such as antibody-testing, monitoring for evidence of infection, the administration of antivirals or immunoglobulin may be considered. Specialist advice should be sought on a case-per-case basis.

In addition, immunisation with live vaccines should be delayed until 6 months of age in children born to mothers who received immunosuppressive biological therapy during pregnancy. In practice, this means that children born to mothers who were on immunosuppressive biological therapy during pregnancy will not be eligible to receive rotavirus vaccine (and will need to defer BCG, if indicated, for 6 months). If there is any doubt as to whether an infant due to receive a live attenuated vaccine may be immunosuppressed due to the mother's therapy, including exposure through breast-feeding, specialist advice should be sought.

Many adults with chronic inflammatory diseases (e.g. rheumatoid arthritis, inflammatory bowel disease, psoriasis, glomerulonephritis) will be on stable long term low dose corticosteroid therapy (defined as up to 20mg prednisolone per day for more than 14 days in adult or 1mg/kg/day in children under 20kg) either alone or in combination with other immunosuppressive drugs. Long term stable low dose corticosteroid therapy, either alone or in combination with low dose **non-biological** oral immune modulating drugs (e.g. methotrexate 25mg per week in adults or up to 15mg/m² in children, azathioprine 3.0mg/kg/day or 6-mercaptopurine 1.5mg/kg/day), are **not** considered sufficiently immunosuppressive and these patients **can** receive live vaccines.

Non-systemic corticosteroids, such as inhalers or topical or intra-articular preparations, do not cause substantial systemic immunosuppression and are therefore not contraindications to administration of live vaccines. Similarly, replacement corticosteroids for people with adrenal insufficiency do not cause immunosuppression and are not, therefore, contraindications for administration of live vaccines.

The 2013 Infectious Disease Society of America (IDSA) Clinical Practice Guideline for Vaccination of the Immunocompromised Host (see further resources) provides further detail for specific vaccines in individuals on specific immunosuppressive therapies. If healthcare professionals administering the vaccine have concerns about the nature of therapies (including biologicals) they should contact the relevant specialist for advice.

Issues concerning vaccines for specific diseases are listed in the appropriate chapters:

- Influenza vaccine (Chapter 19)
- Measles, Mumps and Rubella vaccine (Chapters 21, 23 and 28)
- Rotavirus vaccine (Chapter 27b)
- Shingles vaccine (Chapter 28a)
- BCG vaccine (Chapter 32)
- Oral typhoid vaccine (Chapter 33)
- Varicella vaccine (Chapter 34)
- Yellow Fever vaccine (Chapter 35)

Contact with an individual with immunodeficiency, on current/ recent immunosuppressive therapy (including biologics)

Historically, some live vaccine viruses, including smallpox and oral polio, have been known to transmit and cause harm to close contacts of vaccine recipients with immunodeficiency or on current or recent immunosuppressive therapy. These live vaccines were therefore contra-indicated in healthy household contacts of immunocompromised patients. For most

of the live vaccines used in the current UK schedule, however, transmission to contacts does not occur or can be minimised by simple precautions (see below for vaccine specific advice). In addition, vaccination of close contacts of vulnerable people has a major benefit by reducing the risk of exposure to wild-type infection, and, therefore, some vaccines should be actively encouraged in family and household contacts of those at risk (see chapter 7). Children with immunodeficiency who are attending school do not require exclusion when other children are being immunised.

MMR

Despite extensive international experience, there is no evidence of harm from the transmission of measles, mumps and rubella viruses from recent vaccinees. Therefore, close contacts of immunosuppressed individuals should be fully immunised, against measles, mumps and rubella according to their national schedule.

Rotavirus

Although rotavirus vaccinees do shed viral antigen in their stool, there is no published evidence of harm to household contacts of vaccine recipients. Therefore, eligible close contacts of immunosuppressed individuals should receive rotavirus immunisation according to the national schedule. Where household contacts of immunosuppressed individuals receive rotavirus vaccine, careful hand washing should be used to minimize the risk of transmission of vaccine virus. This will include after handling faeces (e.g. after changing a nappy), and before food preparation or direct contact with the immunocompromised person (Public Health Agency of Canada, 2013).

Varicella Zoster (chicken pox and shingles)

Post-marketing experience with varicella vaccines suggests that transmission of vaccine virus may occur rarely from vaccine recipients who develop a varicella-like rash. Although there is no such evidence of transmission of vaccine virus from recipients of shingles vaccine, it seems plausible that direct contact with vesicular fluid from a recipient with a post-vaccination rash, could lead to transmission. Eligible close contacts of immunosuppressed individuals should therefore be fully immunised against shingles according to the national schedule. Susceptible household contacts of immunosuppressed individuals should also be offered vaccination against varicella to reduce the risk of exposure to chickenpox (chapter 7). Contacts of immunosuppressed individuals who develop a vesicular rash after receiving live varicella or shingles vaccine should attempt to restrict exposure of the vulnerable person (for example by covering a localised rash, or by avoiding face to face contact) until the rash is dry and crusted.

Influenza

Following live attenuated influenza vaccination, vaccine virus has been detected in vaccinees' upper respiratory tracts for periods up to two weeks. There is therefore potential for transmission of the vaccine virus from individuals vaccinated with Fluenz Tetra® to immunocompromised contacts. However, the adaptation of the virus to replicate in the upper respiratory tract, means that harm from this exposure is unlikely. In the US, where there has been extensive use of the live attenuated influenza vaccine, there have been no reported instances of illness or infections from the vaccine virus among immunocompromised patients inadvertently exposed. Annual influenza immunization is therefore recommended for close contacts of immunocompromised persons; the vaccine

used should follow national age-specific recommendations. The exception would be those who cannot avoid contact with severely immunocompromised patients - for example those who would normally be in isolation. Household members and others who cannot avoid contact with very severely immunocompromised patients (e.g. bone marrow transplant patients and others who require isolation) should not be offered live attenuated influenza vaccine but given appropriate alternative inactivated influenza vaccines.

Further information specific to vaccines for specific diseases are listed in the appropriate chapters:

- Influenza vaccine (Chapter 19)
- Measles, Mumps and Rubella vaccines (Chapters 21, 23 and 28)
- Rotavirus (Chapter 27b)
- Shingles vaccine (Chapter 28a)
- Varicella vaccine (Chapter 34)

Pregnancy & breastfeeding

There is no evidence of risk from vaccinating pregnant women or those who are breast-feeding with inactivated virus, bacterial vaccines or toxoids (Plotkin and Orenstein, 2004). Inactivated vaccines do not replicate and so cannot damage an unborn foetus. Some inactivated vaccines (influenza, Tdap-IPV) are actively recommended for pregnant women as they can prevent severe complications during pregnancy or to the new-born infant. Other inactivated vaccines should be administered to pregnant women where protection is required during the pregnancy. If exposure to infection can be avoided until after the mother delivers, deferring vaccination will reduce the chance of any pregnancy complication being incorrectly attributed to vaccine exposure.

Live vaccines are contraindicated during pregnancy as a precaution because of the theoretical risk of foetal infection (Munoz FM, 2013). There has been no evidence to date of direct foetal injury after the administration of live viral vaccines to pregnant women (Munoz FM, 2013). However, since the theoretical possibility of foetal infection exists, live vaccines should generally be delayed until after delivery. Although follow-up of women who have received certain vaccines inadvertently in pregnancy is still underway (<https://www.gov.uk/guidance/vaccination-in-pregnancy-vip>), data are extremely reassuring. Termination of pregnancy following inadvertent immunisation is therefore not recommended.

Immunisation with live vaccines should be delayed for 6 months in children born of mothers who were on immunosuppressive biological therapy during pregnancy. In practice, this implies that children born of mothers who were on immunosuppressive biological therapy during pregnancy will not be eligible to receive rotavirus vaccine (and will need to defer BCG, if indicated, for 6 months). If there is any doubt as to whether an infant due to receive a live attenuated vaccine may be immunosuppressed due to the mother's therapy, including exposure through breast-feeding, specialist advice should be sought".

Temporary deferral of immunisation

There will be very few occasions when deferral of immunisation is required. Minor illnesses without fever or systemic upset are not valid reasons to postpone immunisation. If an individual is acutely unwell (for example with a fever above 38.5 C), immunisation may be postponed until they have fully recovered. This is to avoid wrongly attributing any new symptom or the progression of symptoms to the vaccine. The presence of a neurological condition is not a contraindication to immunisation but if there is evidence of current neurological deterioration, deferral of vaccination may be considered, to avoid incorrect attribution of any change in the underlying condition. The risk of such deferral should be balanced against the risk of the preventable infection, and vaccination should be promptly given once the diagnosis and/or the expected course of the condition becomes clear.

Intervals between vaccinations

Most inactivated vaccines can be given at the same visit or at any time period from each other. Please see Chapter 11 for intervals between vaccines in the routine schedule and relevant chapter for recommendations about specific vaccines.

Where more than one live vaccine is required, earlier guidance recommended that they should be administered on the same day or at four week interval. This advice was based on evidence with measles and smallpox vaccines and supported by the theory that interferon production stimulated by replication of the first virus prevented replication of the second agent, thus leading to an attenuated response. A similar reason was used to explain false negative tuberculin tests in those who had received MMR. More recent evidence suggests that the underlying theory does not hold for all live vaccines, particularly those administered by other routes. Please refer to the relevant chapter for recommendations about specific vaccines.

Deferral of vaccination following immunoglobulin treatment

Immunoglobulins and other blood products may interfere with the immune response to many live vaccine viruses. This is expected because most donors will have antibody to measles, varicella and other common viruses and this antibody may prevent replication of the vaccine virus. If protection is not required imminently, live viral vaccines should therefore be given at least three weeks before or three months after an injection of immunoglobulin. The exceptions to this are below.

Deferral of yellow fever vaccination is not required because immunoglobulins used in the UK are unlikely to contain high levels of antibody to this virus.

Where rubella protection is required for post-partum women who have received anti-D immunoglobulin, no deferral is necessary as the response to the rubella component of MMR is normally adequate.

Deferral of BCG vaccine is not required because immunoglobulins are unlikely to interfere with the cellular response to this vaccine. Therefore, babies who have received hepatitis B immunoglobulin and are eligible for BCG vaccination can receive the vaccine without any deferral.

Where rapid protection is required, vaccination should proceed but may require repetition at a later stage to ensure longer term protection.

False contraindications

The following conditions are **NOT** contraindications to routine immunisation (in some of these situations, additional precautions may be required – refer to the relevant chapter for further information):

- family history of any adverse reactions following immunisation
- previous history of the disease (with the exception of BCG for people who have evidence of past exposure to tuberculosis)
- contact with an infectious disease
- premature birth
- asthma, eczema or hay fever
- mild self-limiting illness without fever, e.g. runny nose
- treatment with antibiotics, topical and inhaled steroids
- child's mother or someone in the household being pregnant
- currently breast-feeding or being breast-fed
- history of jaundice after birth
- under a certain weight
- being over the age recommended in the routine childhood immunisation
- schedule (except rotavirus – see chapter)
- personal history of febrile convulsions or epilepsy
- close family history (parent or sibling) of febrile convulsions or epilepsy
- recent or imminent elective surgery
- imminent general anaesthesia
- unknown or inadequately documented immunisation history: see the algorithm for vaccination of individuals with uncertain or incomplete immunisation status: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/463433/HPA-algorithm-September-2015-04b.pdf
- G6PD deficiency
- food intolerances
- interferons and other non-immunosuppressing immunomodulators

Further resources

- European Group for Blood and Marrow Transplantation www.ebmt.org
- Infectious Disease Society of America. 2013 Clinical Practice Guideline for Vaccination of the Immunocompromised Host. <http://www.idsociety.org/Templates/Content.aspx?id=32212256011>
- Royal College of Paediatrics and Child Health: Immunisation of the Immunocompromised Child, Best Practice Statement (2002) www.rcpch.ac.uk:

- British HIV Association (2015). Guidelines on the use of vaccines in HIV-positive in adults: <http://www.bhiva.org/documents/Guidelines/Immunisation/consultation/BHIVA-Immunisation-Guidelines-2015-Consultation.pdf>
- Children's HIV Association (2015) : vaccination of HIV infected children <http://www.chiva.org.uk/guidelines/immunisation/>

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