

# **Immunosuppression**

Information on pre-travel preparation, tips to stay healthy abroad and links to useful resources for immunosuppressed travellers

## Key messages

- Pre-travel planning is essential; immunosuppressed individuals should discuss their travel plans carefully with their hospital specialist and GP, ideally before booking travel.
- All travellers should obtain comprehensive travel health insurance; immunosuppressed travellers should declare their full medical history to the insurers.
- Immunosuppressed travellers are more likely to experience severe illness as a result of certain infections and extra precautions are recommended. They are also potentially at risk of a deterioration or exacerbation of their condition. The risk may differ depending on the traveller's degree of immune suppression.
- Travellers who are immunosuppressed should be stable, know how to manage their condition, be prepared to manage minor illnesses, and know when and how to seek medical advice abroad.
- Additional vaccines may be recommended for immunosuppressed individuals. Those who are severely immunosuppressed will not be able to have live vaccinations. Inactivated vaccines can be given safely but may be less effective.
- Specific guidelines are available for immunosuppressed children and the vaccination of adult and paediatric haematopoietic stem cell transplant recipients.

#### **Overview**

Immunosuppression is the suppression of the body's normal immune response. This causes a reduced ability to fight infection. Immunosuppression can be caused by a variety of medical



conditions, drugs or treatments.

Risk management advice for the immunosuppressed traveller should follow that of the general traveller and be tailored as outlined below.

- Destination-specific risk management advice can be found on the <u>Country Information</u> pages.
- Comprehensive travel insurance is essential for all travellers. A full declaration of medical conditions should be made to the insurers. All equipment and planned activities should be covered.

## **Immunosuppression**

Immunosuppression can be due to certain medical conditions, or certain drugs or treatment. A list of conditions or drugs/therapies that can cause immunosuppression are shown below. These lists are not exhaustive; health professionals are encouraged to liaise with the traveller's specialist if there is any concern about an underlying medical condition or treatment. For further details see UK Health Security Agency (UKHSA) Immunisation against infectious disease (Green Book) chapter 6 and 7 [1, 2].

## Immunosuppressive conditions

The following groups are considered to have immunosuppression:

- Bone marrow transplant recipients (bone marrow or stem cell transplant) in the past 24 months and until demonstrated not to have on-going immunosuppression or graft versus host disease or in remission following autologous stem cell transplant (transplant using own stem cells). Specialist advice is required in these situations as there will be variation based upon the type of transplant and the immune status of the individual.
- Individuals with acute and chronic leukaemias and lymphoma (including Hodgkin's lymphoma), or under follow up for chronic lymphoproliferative disorder including for example haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma and other plasma cell dyscrasias.
- Some individuals with human immunodeficiency virus (HIV) infection (those living with HIV, with a CD4 count >200/mm/µl [3] and no symptoms of disease are not usually considered to have severe immunosuppression) see our <u>HIV/AIDS factsheet</u> for details.
- Cellular immune deficiencies (e.g. severe primary (inherited) immunodeficiencies, such as severe combined immunodeficiency, 22q11 deficiency/DiGeorge syndrome\*, Wiskott-Aldrich syndrome).
- Antibody deficiencies affecting IgG or IgA associated with T cell deficiencies.\*\*

Certain additional conditions may be associated with immune deficit including those with no spleen and those with a dysfunctional spleen (e.g. some individuals with sickle cell disease or other haemoglobinopathies, some adults with Coeliac disease). These individuals are at increased risk of



overwhelming infection with certain bacterial pathogens and additional vaccinations and standby antibiotics may be required.

Live vaccinations can be offered unless the individual has another immunosuppressive condition/treatment. These individuals are also at risk of severe malaria, and where possible should avoid travel to areas where malaria is a risk.

A number of chronic (long-term) medical conditions (and their treatments) may be associated with varying degrees of immune deficit (e.g. liver disease, kidney disease and diabetes). Additional vaccinations may be recommended for these individuals. Live vaccines can be offered unless the individual has another immunosuppressive conditions/treatment, however, if in doubt specialist advice should be sought.

\*Most patients with 22q11 deletion syndromes are able to receive live vaccines safely provided they have no evidence of being severely immunocompromised [1]. In the case of yellow fever vaccine, as data is limited, a cautious approach is recommended and specialist advice should always be sought.

\*\* Antibody deficiencies affecting IgG or IgA antibodies are not of themselves a contraindication to live vaccination unless associated with T cell deficiencies. In the case of yellow fever vaccine, as data is limited, a cautious approach is recommended, and specialist advice should always be sought.

# Groups considered to be receiving immunosuppressive therapies

- Those who are receiving or have received in the past 12 months immunosuppressive biological therapy (e.g. anti-TNF drugs such as alemtuzumab, ofatumumab, rituximab, etanercept, infliximab and adalimumab) unless otherwise directed by an expert.
- 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 on the type of transplant and the immune status of the patient).
- Those who are receiving or have received in the past 3 months: high-dose corticosteroids or immune modulating drugs including:
  - >40mg of prednisolone (or an equivalent drug) a day for more than one week in adults, or 2mg/kg/day of prednisolone (or an equivalent drug) in children under 20 kg for at least one week
  - >20mg prednisolone (or an equivalent drug) a day for more than 14 days in adults or 1mg/kg/day in children under 20kg
  - 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
  - children on non-biological oral immune modulating drugs (except those on low doses, see 'Green book' chapter 6) [1]



The list of immunosuppressive therapy is vast. The following are examples of immunosuppressive drugs not already mentioned that are commonly encountered in practice. Specialist advice should always be obtained if there is any doubt.

- Ciclosporin
- Cyclophosphamide
- Leflunamide
- · Mycophenolate mofetil
- Sirolimus
- Tacrolimus

The lists above are not exhaustive; health professionals should liaise with the supervising doctor where there is any concern about the possible immunosuppressive effects of a medication.

When considering administration of yellow fever vaccine, limited data is available on safety for those on lower dose immunosuppressive therapies, a cautious approach is advised, and specialist advice should be sought.

Medications **not** usually linked to immunosuppression include:

- Non-systemic corticosteroids, such as aerosols, skin creams and intra-articular (joint) injections.
- Steroid replacement therapy for adrenal insufficiency (Addison's disease).
- Other drugs used in autoimmune and inflammatory conditions include aminosalicylates (mesalazine and sulphasalazine) and hydroxychloroquine (anti-inflammatory). These drugs are not considered directly immunosuppressive and do not usually contraindicate live vaccines. However, the traveller's underlying medical condition must also be taken into account when considering if an individual is immunosuppressed.

For further details see <u>contraindications and special considerations</u> in UKHSA Immunisation against infectious disease (Green Book) [1].

# **Pre-travel preparation**

Immunosuppressed travellers should be advised to research their destination/s in detail and discuss their travel plans carefully with their supervising specialist, ideally before booking travel. Information can be found on our <u>Country Information</u> pages and the <u>Foreign, Commonwealth & Development Office</u> website.

Travellers should have a plan of what to do should they become ill whilst travelling and need to seek medical help. Travel insurance covering the immunosuppressive condition and/or treatment should be obtained. Support groups for the specific condition may be able to provide advice on where to obtain specialist insurance (see resources below for some of these groups).



Travellers should carry a first aid kit tailored to their destination to help them manage common issues such as insect bites, cuts and grazes, travellers' diarrhoea or headache.

Specific issues to address pre-travel include:

- Is the individual fit to travel/fly?
- Is the immunosuppressive condition and/or treatment stable?
- Can specific interventions (e.g. behavioural measures, vaccination or preventative medication) be recommended to reduce disease risks?
- Does the condition/treatment contraindicate or decrease effectiveness of any recommended vaccines and/or malaria chemoprophylaxis (antimalarials)
- Is appropriate specialist emergency care available at the destination?
- Does the individual have comprehensive travel insurance which covers travel when immunosuppressed?

#### Medication

Travellers who take regular medication should plan well ahead. A letter from the GP or prescriber detailing the medicines is advised. Some countries may not allow the entry of certain types of medicines, and others may have regulations requiring specific permission for a medication to be brought in. These rules can also apply to medicines available over the counter in the UK. Counterfeit (fake) drugs are more common in certain regions and can be a significant health risk. Further information can be found in our medicines and travel factsheet.

When prescribing antibiotics, antimalarials or any other medication, all potential interactions with immunosuppressive drugs (or antiretroviral medicines for those living with HIV) must be considered. The <u>British National Formulary</u>, the <u>University of Liverpool HIV drug interactions</u> website and the <u>electronic medicines compendium</u> are all useful tools for checking potential drug interactions.

#### **Vaccination**

Individual assessment of a traveller's immune status is required before planning travel vaccinations.

- All travellers should be up to date with inactivated vaccines in the UK schedule.
- Inactivated vaccines are safe to administer and should be offered where appropriate.
  However, the immune response may be compromised (reduced) resulting in less-than
  optimal protection. Immunosuppressed individuals should be counselled about this and
  encouraged to further reduce their risk by taking additional preventive measures e.g. insect
  bite precautions and personal and food and water hygiene should be stressed. For some
  travellers, additional doses of vaccine maybe recommended.
- Due to the potential for a reduced response to vaccination, vaccine schedules are sometimes different and post-vaccination serology may be recommended to guide booster



frequency.

Individuals who receive bone marrow or stem cell transplants are likely to lose any natural or immunisation-derived protective antibodies against most vaccine-preventable diseases. National and International guidance recommends that stem cell transplant recipients are considered 'never vaccinated' [4]. All individuals should be considered for a re-immunisation programme. Inactivated vaccines are considered safe in this population. Live vaccines should be delayed until specific criteria regarding immune status are met and should follow guidance detailed in the Green Book, Chapter 6. Specialist advice should be sought to ensure that vaccination is given appropriately [2, 4]

Vaccination schedules for those following stem cell transplant may differ from those in the routine immunisation programme and are detailed in a 'Joint consensus statement on the vaccination of adult and paediatric haematopoietic stem transplant recipients'[4].

#### Live vaccines

Those who are severely immunosuppressed will not be able to have live vaccinations. Live vaccines currently used in the United Kingdom include Bacillus Calmette-Guérin (BCG for TB prevention), dengue vaccine (Qdenga®), paediatric nasal influenza, mumps, measles and rubella (MMR), oral typhoid, rotavirus, shingles, varicella (chickenpox) and yellow fever (YF).

Travellers with relatively minor immunodeficiencies can receive all recommended vaccinations, including live vaccines. Live vaccines are however contraindicated for those who are severely immunosuppressed, as they can cause severe or fatal infections due to extensive replication of the vaccine strain following administration. Where there is doubt about an individual's immune status, specialist advice should be obtained [1].

Please note when considering administration of YF vaccine, limited data is available on safety for those on lower dose immunosuppressive therapies, a cautious approach is therefore advised, and specialist advice should be sought.

YF vaccine can be considered for those living with HIV, depending on immune status of the individual, see our <u>HIV/AIDS factsheet</u> for details [3, 5, 6].

If healthcare professionals administering the vaccine have queries about a patient's level 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 [1].

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 [1]. However, as the vaccine viruses are generally attenuated (weakened) immunosuppressive treatment should



not be delayed if this could result in worsening of the underlying condition. Specialist advice should be sought on a case-per-case basis [1].

#### Food and water risks

Travellers' diarrhoea is the most common illness that affects travellers to low-income regions of the world [7]. Some food and water-borne illness such as those caused by *Salmonella*, *Campylobacter*, *Giardia*, *Listeria* and *Cryptosporidium* can be severe or become chronic (long-lasting) in immunosuppressed individuals [8].

Immunosuppressed travellers should take particular care with <u>food and water hygiene</u> and discuss the management of diarrhoea with their health care provider. Travellers should be given clear advice and written instructions on the appropriate use of self-treatment medication. A prescription for an antibiotic for self-treatment should be considered, details are available in our <u>travellers'</u> <u>diarrhoea factsheet</u>. Prompt treatment of gastrointestinal infection is essential in immunosuppression and specialist advice should be sought, if available locally.

Prophylactic antibiotics may also be considered for some immunosuppressed travellers, especially for short-term travel. The choice of agent must be balanced with possible drug interactions and location of travel [9]. Potential drug interactions should be carefully checked by the prescriber.

#### **Vector-borne risks**

Immunosuppressed travellers should take particular care to <u>avoid insect bites</u>. Travellers should avoid scratching bites and keep them clean and dry to avoid infection. Antihistamine and basic wound dressings can be helpful if the bite is causing irritation. Prompt medical advice should be sought if signs of skin infection develop.

Certain other insect-borne diseases such as visceral leishmaniasis [8] and Chagas disease [9] may also be more severe for immunosuppressed travellers.

There is little published information on the <u>risk of Zika virus for those with immunosuppression</u>, guidance is available from UK Health Security Agency (formerly Public Health England) [10].

Ideally, severely immunosuppressed travellers should avoid travelling to yellow fever (YF) risk regions as the vaccine is contraindicated. Realistically, some may feel they have compelling reasons to travel and be determined to go. These travellers should be counselled about reducing their risk as much as possible by practising scrupulous mosquito bite avoidance and minimising time spent in risk areas. Where travel to a YF risk country cannot be avoided and where an International Certificate of Vaccination or Prophylaxis is needed for entry to that country, a Medical Letter of Exemption (MLoE) from YF vaccination can be offered when YF vaccination is contraindicated on medical grounds. A MLoE should be taken into consideration by the destination country but may not guarantee entry.



#### Malaria

Travellers with immunosuppression can have a higher risk of severe malaria [9]. Travel to malaria endemic areas should be considered carefully. Travellers should be familiar with the 'ABCD' of malaria prevention. Strict bite avoidance measures and compliance with malaria chemoprophylaxis (antimalarials) is necessary. All potential drug interactions should be determined when prescribing antimalarials. Drug information should be checked in the British National Formulary (BNF) and at www.hiv-druginteractions.org

In low-risk areas, where antimalarials are not routinely recommended, they may be considered in exceptional circumstances for immunosuppressed travellers.

Travellers with an absent or poorly functioning spleen should be dissuaded from travel to any area with risk of malaria, but where travel is essential awareness, rigorous bite avoidance and antimalarials should be advised.

In these circumstances, specialist advice may be helpful. Further information is available in the UK Health Security Agency (UKHSA) Malaria prevention guidelines for travellers from the UK.

#### COVID-19

Those with a weakened immune system are at increased risk of severe COVID-19 disease. All individuals should follow <u>current UK recommendations</u> to reduce their risk of catching COVID-19 and passing it on to others.

Those who are more severely immunosuppressed may not make a good immune response to COVID-19 vaccinations. For these individuals, <u>enhanced protection measures should be followed</u>.

Immunosuppressed travellers should assess their individual circumstances, including medical facilities at their destination and consider whether postponing travel would be appropriate.

<u>UK Health Security Agency (UKHSA) Immunisation against infectious disease, the 'Green Book' COVID-19 chapter</u> gives detailed advice about different ages, clinical risk groups and eligibility for COVID vaccination.

General guidance regarding <u>risk assessment for travel</u> during the COVID-19 pandemic and information about the <u>COVID-19 vaccination programme</u> is available.

#### Other health risks

Travellers with immunosuppression should be aware of diseases of close contact, respiratory infections such as tuberculosis and influenza and those transmitted by animal bites such as rabies and wound infections.



Respiratory fungal infections, such as Cryptococcus, Histoplasma, Paracoccidioides and Penicillium are rare, but can cause life-threatening opportunistic infections in immunosuppressed travellers. Caving and other outdoor activities that put travellers at risk should be avoided [9]. Exposure to dust, soil, and bird or bat droppings should also be avoided. Masks and gloves can help reduce exposure to fungal spores if working with plants, hay or peat moss.

#### Venous thromboembolism

Venous thromboembolism (VTE) (deep vein thrombosis or pulmonary embolism) can occur as a result of long periods of immobility associated with any form of travel. Some travellers are at increased risk e.g. older travellers, those with cancer or a previous history of VTE or recent surgery. Those at increased risk of VTE should seek advice from their health care provider and consider the use of properly fitted compression socks. Low molecular weight heparin therapy may also be recommended. Further information is available in our venous thromboembolism factsheet.

## Sun protection

Travellers with immunosuppression should take particular care in the sun. Immunosuppressive treatments have the potential to impair the skin immune system leading to an increased incidence of skin cancer [11]. Certain medications can make skin more sensitive to the sun and more likely to burn. Travellers should seek urgent medical advice if they notice changes to moles, such as increasing size, itchiness, bleeding or oozing, or if a new mole develops very quickly.

# Soil-transmitted helminth (worm) infection

Helminth infections are caused by different species of parasitic worms. Infection may be transmitted through ingesting helminth eggs or, in some cases, penetration of the worm larvae through the skin [12]. Travellers should follow good <u>food</u>, <u>water</u> and personal hygiene advice and avoid walking barefoot on soil/sand.

Most travellers will be at very low risk from soil-transmitted helminth infections. However, overwhelming infection with <u>Strongyloides stercoralis</u> can occur in travellers who are immunosuppressed. If visiting tropical/subtropical areas, travellers with immunosuppression should be discouraged from walking barefoot. Prompt medical advice should be sought if infection is suspected, as early treatment could prevent severe illness [13].

#### Illness abroad

Travellers should know when and how to seek prompt medical advice, for example if they experience fever, prolonged diarrhoea, signs of dehydration, signs of skin infection such as swollen, painful / red skin around a wound with pus, or any other concerning symptoms.

Prophylaxis with immunoglobulins other antibiotic or antiviral drugs may be recommended for



immunosuppressed individuals exposed to infections such as measles, chickenpox, hepatitis A, pertussis (whooping cough) or influenza. Advice on the management of exposed individuals can be found in <u>Chapter 7 of the Green Book</u>.

Travellers should keep any receipts for treatment and the travel insurance company should be informed as soon as possible. In European Union (EU) countries, travellers should carry a <u>European Health Insurance Card (EHIC)</u> or a <u>Global Health Insurance Card (GHIC)</u> as this will allow access to state-provided healthcare in some countries, at a reduced cost, or sometimes for free. The EHIC or GHIC, however, is not an alternative to travel insurance. Check the <u>GOV.UK</u> website for guidance.

#### Resources

- British Association of Dermatologists: Leaflet on immunisation recommendations for children and adult patients treated with immune-suppressing medicines
- Cancer Research UK: Travel Insurance
- HIV and AIDS
- Macmillan cancer support: Finding travel insurance
- Medicines and travel
- Sun protection
- Pinto MV, Bihari S, Snape M.D,(British Infection Association) Immunisation of the immunocompromised child, Journal of Infection (2016) 72, S13eS22
- UK Health Security Agency: Splenectomy information for patients
- Terrence Higgins Trust: Companies offering travel insurance for people with HIV
- <u>US Centers for Disease Control and Prevention: Immunocompromised Travellers</u>
- Public Health England Zika virus and immunocompromised patients

#### REFERENCES

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