Vulnerable Groups and Travel Health Considerations

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Abstract Renowned speaker and author Denis Waitley states that "Life is inherently risky" and travel may be associated with additional risks, particularly to health. The nature of these health risks depends on environmental and host factors. In this chapter we focus on the latter, particularly factors related to physiological vulnerabilities or pre-existing conditions (as opposed to particular risk behaviours). We consider vulnerable travellers to be those at relatively increased risk of travel-related health problems and/or who face particular challenges or issues while travelling. Vulnerable traveller groups include children, pregnant and breastfeeding women, older adults, travellers with pre-existing diseases, physically challenged travellers and the immunocompromised. While travel is rarely contraindicated for these groups, pre-travel consultation with a health practitioner is essential to ensure that risks are evaluated, and appropriate precautions taken. In this chapter, we discuss the literature pertaining to travel health risks in these vulnerable groups, and specific considerations with regard to prevention and management of infection, injury, and other health issues that may be encountered while abroad.

Keywords Travel · Health · Vulnerable groups · Medical conditions · COVID-19

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J. Wilks et al. (eds.), *Tourist Health, Safety and Wellbeing in the New Normal*,
https://doi.org/10.1007/978-981-16-5415-2_4

Introduction

Vulnerability can be defined as the degree to which an individual or group is susceptible to physical or emotional harm. Travellers may be considered *vulnerable* if they are at increased risk of travel-related health problems or face particular issues or challenges related to travel. Amongst tourist travellers, vulnerable groups that warrant special consideration include those listed in Table 1. The increasing accessibility and convenience of travel mean that these groups are able to travel further and wider than ever before. However, specific considerations exist for these groups in relation to risk communication, pre-travel preparation and access to medical care or special equipment during travel. The evidence base for guiding risk-reduction in these groups is more limited than for other travellers, largely resulting from their

Table 1 Vulnerable traveller groups

Group	What makes them vulnerable?
Children	Increased susceptibility to/severity of some infections (including malaria, tuberculosis and rabies) More susceptible to variations in temperature and dehydration and more likely to be bitten by animals than adults Precautions/contraindications exist for some vaccines and medications, particularly in young children (many vaccines have lower age limits)
Pregnant and breastfeeding women	Increased susceptibility to/severity of some infections (e.g., malaria, hepatitis E, influenza, travellers' diarrhoea) Increased risk of venous thromboembolism Risk of obstetric complications Limited safety data for some vaccines and medications Contraindications for some vaccines and mediations
Older adults	Greater likelihood of underlying medical conditions, physical and sensory limitations Increased risk of illness, injury or death while travelling, even in the absence of pre-existing medical problems Increased severity of some infections (e.g., influenza, COVID-19, hepatitis A, encephalitis) Reduced efficacy and immunogenicity of some vaccines Increased risk of yellow fever vaccine-related adverse events Increased risk of stress, panic (e.g., associated with mental impairment, general slowdown)
Travellers with pre-existing disease	Heterogenous group with differing levels of vulnerability May be at increased susceptibility to/severity of some infections (e.g., influenza, COVID-19) More likely to require medical attention during travel
Physically challenged travellers	May require assistance on certain forms of transportation and/or special accommodations or services that may not be easily available in some areas
Immunocompromised travellers	Increased susceptibility to/severity of some infections Reduced efficacy and immunogenicity of some vaccines Precautions/contraindications for some vaccines

frequent exclusion from research studies due to concerns regarding risk and generalisability.

The COVID-19 pandemic has highlighted the particular vulnerability of certain groups to symptomatic and serious COVID-19 illness. There is substantial overlap between the vulnerable traveller groups outlined in Table 1, and groups at increased risk for severe COVID-19 illness, which include older adults, those with pre-existing conditions and the immunocompromised. In this chapter, we will review the literature relating to each of these vulnerable groups in the context of COVID-19 and other travel-related risks or issues and discuss specific pre-travel considerations for each group in the *new normal*.

In all vulnerable groups it is paramount to have travel health insurance that covers the travellers' particular vulnerability and includes cover for hospitalisation abroad and repatriation, even if it is costly and challenging to obtain (Askling & Dalm, 2014; Hezelgrave et al., 2011).

The Paediatric Traveller

An estimated 7% of international travellers are infants and children; their main reasons for travel are tourism and visiting friends and relatives (VFR) (Hagmann et al., 2010). Infants and small children are more susceptible to infections such as travellers' diarrhoea (TD), and diarrhoeal illness accounts for an increased proportion of travel-related diagnoses with increasing age (Hunziker et al., 2012). Children may also be prone to more serious complications than adults (Garbash et al., 2010) and require hospitalisation more often. Malaria is associated with a case fatality ratio of <0.4% (Stager et al., 2009). Children are more likely than adults to play with, pat or feed animals, and are therefore at higher risk of rabies (Gautret et al., 2015; Hagmann et al., 2010). Children suffer a higher proportion of motor vehicle related deaths abroad (Guse et al., 2007), with accidents the leading cause of mortality in young travellers (Stewart et al., 2016).

Prior to deciding whether to travel with infants and small children, caregivers must assess whether pleasure and benefits outweigh discomfort and risks (Summer & Fischer, 2019). Caregivers must be prepared to be far more vigilant than at home, and should avoid overloading the programme and ensure they offer children plenty of time to play and relax (Stauffer et al., 2001). Most children dislike vaccine injections, long flights and extreme temperatures, whereas they usually like animals, action and entertainment, an altered horizon, family cohesiveness and the opportunity to share some special stories with friends.

Most children are in good health and do not need medication, but some may have special needs (Kohl & Barnett, 2020). Absolute contraindications to travel are rare, but air travel should be avoided with <2 week-old infants. Caregivers should be discouraged from taking very young children on vacation to countries highly endemic for tropical or infectious diseases; the WHO discourages travelling with children to malaria endemic areas. Similar precautions and contraindications exist

for children with a history of pre-existing conditions, immunosuppressive medication or recent surgery as for adults. There is inconsistent evidence relating to a greater risk of acute mountain sickness in children (Wu et al., 2018).

COVID-19 in Children

Based on literature published to date, children tend to have milder COVID-19 disease and better prognosis than adults (Gotzinger et al., 2020; Ludvigsson, 2020). COVID-19 may go undetected in children, with risk of transmission to adults in the travelling party while undiagnosed. Nevertheless, a small proportion of children will require hospitalisation and intensive care due to COVID-19 and its complications, such as the rare but emerging entity of multisystem inflammatory syndrome in children (Consiglio et al., 2020; Jiang et al., 2020; Feldstein et al., 2021).

Pre-Travel Paediatric Counselling

Overall advice should include the same topics as for adults, but attention must be paid to some special aspects. The primary reason to seek a pre-travel consultation is usually immunisation—this is a perfect opportunity to update missing routine immunisations as per national recommendations. Depending on the destination and other trip characteristics, additional travel vaccines may be indicated, particularly those against rabies, hepatitis A and possibly typhoid (Steffen & Hamer, 2020). Detailed recommendations have previously been published (Slonim et al., 2014; Starr, 2013; Torresi et al., 2019). Concerns exist about non-adherence to such recommendations, particularly by VFR families (Decuyper et al., 2019).

If travelling to malaria-endemic areas, malaria prophylaxis is paramount in this age group, and detailed advice relating to personal protection measures against mosquito bites is the first line of defence (Korzeniewski, 2018). Repellents containing N, N-diethyl-meta-toluamide (DEET) in a concentration ≤30% can be applied safely (Stanczyk et al., 2015; Swale & Bloomquist, 2019). Repellents should be washed off following return to a protected indoor area. Malaria chemoprophylaxis for children follows the same basic rules as for adults. Atovaquone-proguanil (Malarone) is now the first choice for children with a weight of ≥11 kg; the number of paediatric tablets must be adapted to the body weight. Mefloquine can be given to children ≥5 kg and tends to be better tolerated by children than adults. Doxycycline is contraindicated for children <8 years (<12 years in the UK) (Hagmann & Schlagenhauf, 2011; Kafai & Odom John, 2018).

TD is common in children and may develop into a major problem (Chong et al., 2019). Even though there is no evidence for effectiveness, we recommend strict

food and drink hygiene for children. As diarrhoea can become life-threatening within a few hours in children, rapid intervention in the form of rehydration (via the oral route if possible) is indicated. Consultation with a paediatrician or family physician is prudent, particularly if the child is not tolerating oral fluids, as hospitalisation will often be necessary (Ashkenazi & Schwartz, 2020; Torresi et al., 2019). In most countries loperamide (Imodium) is contraindicated for those aged <6 years (some countries <2 or <12 years), and there is increasing reluctance to use antibiotics (Ashkenazi & Schwartz, 2020; Leshem, 2020).

Children are more susceptible to motion sickness than adults. Commonly used medications include diphenhydramine and dimenhydrinate. Scopolamine and various other agents should be avoided in those aged <12 years, owing to increased risk of side effects. On planes, small children often develop earaches during descent as they lack knowledge on how to air the middle ear through the Eustachian tube. Drinking, yawning, or chewing gum may offer relief. In contrast, children usually get over jet lag much faster than do adults (Stauffer et al., 2001).

Travelling children are susceptible to accidents. To ensure car safety, special seats must be carried or ordered in advance and seatbelts must be used. Children must be educated on how to carefully cross streets in countries where driving patterns are different, particularly if the traffic comes from the opposite side of the road to that which is familiar to them. They must abstain from petting animals (Ashley et al., 2019). Supervision on the beach and in the swimming pool is paramount, as drowning is the second leading cause of death in paediatric travellers (Sleet & Balaban, 2013). Swimming pools in developing countries with hot climates bear a higher risk of ear infections due to bacterial and fungal contamination. Excessive chlorination of water may cause conjunctivitis. Children who stay in the pool for prolonged periods of time should wear protective goggles and earplugs. In developing countries, hotel rooms should be checked for potential hazards; specifically, open electrical wiring and sockets, paint chips, pest poisons or traps, and low or unstable balcony railings. Adolescents must be warned about sexually transmitted infections and drugs (Guilamo-Ramos et al., 2015).

Children are more susceptible to environmental hazards, particularly related to climate. To prevent heat injuries, caregivers should limit physically demanding daytime activities, minimise direct sun exposure and ensure that children maintain hydration and wear loose-fitting and light clothing. Sunscreen should be applied often and liberally in hot climates and during periods outdoors, as melanoma risk is more than doubled in individuals who have had one or more episodes of severe sunburn in childhood. In cold climates, caregivers should ensure that children wear layered clothing and gloves and woollen socks to prevent cold injuries. Layers should include an underwear layer that takes away moisture, an insulating layer (e.g., wool or fleece), and an outside shell (e.g., nylon). Appropriate footwear should be worn at all times, particularly on the beach (Stauffer et al., 2001).

Pregnant and Breastfeeding Women

Travel during pregnancy is increasingly common (Antony et al., 2017) and pregnant women appear just as likely to travel to high-risk destinations as other travellers (Hagmann et al., 2017; Hochberg et al., 2013; Jaeger et al., 2015). Pre-baby getaways are a growing tourism trend, with the concept of a *babymoon* (a holiday taken by parents-to-be before their baby's birth) now firmly ensconced in popular culture (Gallivan et al., 2019).

Pregnancy is associated with a range of hormonal, anatomical and physiological changes that increase susceptibility to certain travel-related health risks (Antony et al., 2017). These include increased vulnerability to travel-related infections such as malaria, influenza and Zika; heightened risk of venous thromboembolism (VTE) with long-distance journeys; and the risk of an obstetric mishap far from home and reliable (or familiar) medical care. Due to concerns regarding risks to mother and foetus, pregnant women are often excluded from randomised trials. Recommendations are therefore often based on small observational studies or extrapolated from non-pregnant travellers, and vaccine and medication safety data is often limited (Antony et al., 2017; Nasser et al., 2020).

Epidemiological Evidence for Health Problems in Pregnant Travellers

Physiological changes in pregnancy, including changes to the immune system, may increase susceptibility to or severity of infections (Kourtis et al., 2014). Pregnant women are at increased risk of influenza and its complications, including critical illness and neonatal morbidity and mortality (ANZIC Influenza Investigators, 2010; Mertz et al., 2017). Malaria in pregnancy is often more severe, and may be associated with pregnancy complications such as low birth weight and foetal loss (McKinney et al., 2020). Amongst pregnant travellers, VFR travellers are at highest risk for acquiring malaria, with most cases imported from West Africa (Kaser et al., 2015; Mace et al., 2019). Hepatitis E virus infection in pregnancy may follow a fulminant course, with hepatic failure and pregnancy complications such as membrane rupture and foetal loss (Perez-Gracia et al., 2017). Infection by *Listeria monocytogenes* during pregnancy may result in foetal loss, preterm birth, or invasive disease in the newborn (Madjunkov et al., 2017). Another concern for pregnant travellers is Zika virus, which can be vertically transmitted, leading to congenital microcephaly, other congenital abnormalities, or foetal loss (Pomar et al., 2019; Vouga et al., 2019). Maternal Zika infections in the first trimester appear to be associated with more severe foetal adverse outcomes (Vouga et al., 2019). Most maternal Zika infections are asymptomatic and associated with low rates of maternal complications comparable to other adults (Flamand et al., 2017; Honein et al., 2017). Infection with rubella or varicella during pregnancy can lead to complex

congenital anomalies; pre-pregnancy rubella and varicella vaccination is indicated for non-immunes (Swamy & Heine, 2015).

Delayed gastric emptying and increased intestinal transit time during pregnancy may result in more severe dehydration and ketosis with TD, increasing the risk of premature labour (Agnew et al., 1993; Hezelgrave et al., 2011). The tendency to nausea and vomiting in early pregnancy may be aggravated by travel, particularly by activities prone to motion sickness (Carroll & Williams, 2008).

Prothrombotic changes to the endothelium and relative obstruction to venous flow by the gravid uterus increase the risk of VTE in pregnancy (Hezelgrave et al., 2011). While specific data about travel-related VTE in pregnant women is limited (Izadi et al., 2015), studies in non-travellers suggest that VTE is five to ten times more common in pregnant women compared to matched non-pregnant controls, and complicates about one in a thousand pregnancies (Hezelgrave et al., 2011; Kourlaba et al., 2016). Pregnancy is associated with increased weight gain, decreased abdominal muscle strength, increased joint laxity and spinal lordosis, which shift a pregnant woman's centre of gravity and alter postural balance (Cakmak et al., 2016). This places pregnant women at greater risk for falls, especially during activities that require extreme balance, coordination and agility. Falls during pregnancy may result in maternal and foetal complications including maternal bone fractures, head injuries, placenta abruption, and rupture of the uterus and membranes (Cakmak et al., 2016).

Pregnancy and COVID-19

Published evidence on the impact of COVID-19 in pregnant women and their babies remains limited (Khalil et al., 2020). Based on existing evidence, perinatal and maternal mortality due to COVID-19 appears to be rare (<1%) (Khalil et al., 2020; Vouga et al., 2021; Ellington et al., 2020). However, emerging data suggests that pregnancy is a risk factor for hospitalisation and more severe COVID-19 illness, and that women who experience COVID-19 in pregnancy are at increased risk of maternal morbidity, mortality and neonatal complications compared to pregnant women without COVID-19. Reported risk factors for severe COVID-19 in pregnancy include older maternal age, pre-existing medical problems (including hypertension and diabetes), high body mass index, and non-white ethnicity (Khalil et al., 2020; Knight et al., 2020; Allotey et al., 2020; Villar et al. 2021; Vouga et al., 2021). Obstetric and neonatal outcomes are influenced by the severity of maternal disease, with an increased risk of caesarean section, preterm birth and neonatal admission to the intensive care unit observed among pregnant women with severe disease. (Khalil et al., 2020; Knight et al., 2020; Vouga et al., 2021). Although some reports suggest that the virus causing COVID-19 may be transmitted from mother to baby, this appears to be rare (Khalil et al., 2020). In babies born to COVID-19 positive mothers, perinatal transmission is unlikely to occur if correct hygiene precautions are undertaken and breastfeeding is safe when paired with effective parental education

of strategies to protect the infant (Salvatore et al., 2020). While high rates of thrombotic complications have been reported in patients hospitalised with COVID-19 (Klok et al., 2020; Middeldorp et al., 2020) and concerns exist about the potential for increased risk in pregnancy, data published to date do not signal an increased risk of VTE in pregnant women with COVID-19 (D'Souza et al., 2020).

Travel Health Advice for Pregnant and Breastfeeding Travellers

Pre-travel preparation for the pregnant traveller should start with a review of her obstetric and medical history and planned travel itinerary. Travel is rarely contraindicated during a normal pregnancy, but the presence of certain obstetric or medical risk factors or planned travel to hazardous destinations (Table 2) warrants consultation with an obstetrician, often in conjunction with a medical specialist, regarding the advisability of the proposed itinerary (Hezelgrave et al., 2011).

The safest time for a pregnant woman to travel is generally during the second trimester, as the most common obstetric emergencies occur in the first and third

Table 2 Potential contraindications to travel during pregnancy

Obstetric risk factors	
Absolute contraindications	**Relative contraindications**
Placental abruption Active labour or pre-term labour Cervical insufficiency Premature rupture of the foetal membranes Suspected ectopic pregnancy Threatened abortion with vaginal bleeding History of or current eclampsia	Multiple gestation, placental abnormality, or foetal growth restriction in present pregnancy History of miscarriage, ectopic pregnancy, pre-term birth or premature rupture of foetal membranes Maternal age >35 or <15 years of age
Medical risk factors	
Severe anaemia or haemoglobinopathy Symptomatic valvular heart disease, unstable angina or congestive cardiac failure Pulmonary hypertension, cystic fibrosis, pneumothorax or bullous lung disease Poorly controlled asthma, epilepsy or diabetes Other chronic medical problems requiring frequent medical assessment or interventions History of venous thromboembolism	
Hazardous destinations	
High altitude (≥3000m) Areas endemic for malaria (particularly mefloquine-resistant *P. falciparum* malaria) or hepatitis E Areas with ongoing Zika virus transmission Areas with active outbreaks of infections for which there is increased maternal or foetal risk Areas where live virus vaccines are required or recommended	

Source: Adapted from Antony et al. (2017) and Hezelgrave et al. (2011)

trimesters (American College of Obstetricians and Gynecologists [ACOG] Committee, 2018). First trimester complications such as miscarriage and ectopic pregnancy can be disruptive, costly, and potentially life-threatening. When travel during the first trimester is planned, a pre-travel ultrasound should be recommended to confirm the pregnancy's location and the presence of a foetal heartbeat (Antony et al., 2017). In the third trimester, the biggest risk is that of pre-term delivery. Women planning travel during pregnancy should consider the availability of maternity and neonatal care facilities at their destination (Easa et al., 1994).

Occasional air travel is considered safe for pregnant women without obstetric or medical complications (ACOG Committee, 2018). Radiation protection authorities recommend a maximum exposure of 1mSV of radiation over the course of a pregnancy, which equates to about 200 h of flying (Antony et al., 2017). Most airlines require pregnant women to carry a letter from a registered medical practitioner or midwife after 28 weeks documenting the status of the pregnancy and the expected delivery date. Air travel is generally discouraged after 36 weeks (or after 32 weeks for a multiple pregnancy). As regulations vary, women should be advised to check with their airline before flying. Due to the increased risk of VTE, pregnant travellers should be advised about measures aimed to reduce VTE risk, such as choosing an aisle seat, taking regular walks around the cabin, frequent exercises of the legs and feet, drinking plenty of fluid (not containing alcohol or caffeine), avoiding restrictive clothing and wearing graduated compression stockings (Royal College of Obstetricians and Gynaecologists, 2013).

Certain activities, such as sports for which the risk of injury is high (e.g., downhill skiing), or where there is risk of significant changes in atmospheric pressure (e.g., scuba diving), may need to be restricted or avoided during pregnancy (Table 3).

Practitioners should review safety data and relevant categorisation systems prior to administering or prescribing any vaccine or medication to a pregnant or breastfeeding woman.

Table 3 Activities that may need to be restricted or avoided during pregnancy

Activity	Risks and recommendations in pregnancy
SCUBA diving	Not recommended due to risks to foetus (Conger & Magann, 2014); inadvertent exposure in early pregnancy is not a reason for pregnancy termination (Reid & Lorenzo, 2018)
Downhill skiing, horse riding, skating	Not recommended in the second half of pregnancy due to injury risk (Jean & Moore, 2012)
Water-skiing	Not recommended during pregnancy due to risk of injury and peritonitis (Cooper, 2006)
Cruise ship travel	Gestational age limit for most cruise lines is 24 weeks (Dahl, 2007); risks include influenza and gastroenteritis outbreaks, motion sickness and falls; cruise ships also have limited resources for managing an obstetric emergency (Morof & Carroll, 2017)
Altitude	Travel to sleeping altitudes of ≥3000m is not recommended (Jean & Moore, 2012; Mieske et al., 2010)

Vaccination during pregnancy has benefits for the mother, and may also benefit the foetus through passive immunity (transplacental transfer of maternal antibodies) (Swamy & Heine, 2015). With the exception of smallpox vaccination, which has been associated with congenital defects and foetal loss (Badell et al., 2015), there is no clear evidence that any vaccine (inactivated or live) poses a risk during pregnancy (Nasser et al., 2020). However, vaccine safety data in pregnant women is typically limited, and live vaccines are generally avoided due to theoretical risks to the foetus (Nasser et al., 2020; Swamy & Heine, 2015). Inactivated influenza and pertussis vaccines are considered safe and are recommended for all pregnant women (Hall et al., 2020a; Nasser et al., 2020; Swamy & Heine, 2015). Administration of other vaccines may be considered in situations where exposure is likely and the benefits outweigh the risks (i.e., disease poses a greater risk to the woman or foetus than the vaccination) (Antony et al., 2017; Nasser et al., 2020). If there is a choice between a live and an inactivated vaccine (e.g., polio, typhoid), the inactivated one should be administered (Cooper, 2006). As yellow fever vaccine is a live vaccine for which limited safety data exists in pregnancy, pregnant women should be advised to avoid or postpone travel to yellow fever risk areas (Hall et al., 2020b; Reno et al., 2020). However, if travel cannot be avoided, yellow fever vaccination is recommended for pregnant women travelling to endemic areas (Staples et al., 2010; World Health Organization [WHO], 2013).

Pregnant women should be counselled about the risk of travel-related mosquito-borne diseases including Zika and malaria. Pregnant women who do not reside in Zika transmission risk areas should be advised to avoid travel to risk areas (Vouga et al., 2019). If travel cannot be avoided, advice on how to prevent mosquito bites and sexual transmission should be provided. Similarly, travel to malaria-endemic areas should be avoided during pregnancy when possible (McKinney et al., 2020). If travel is unavoidable, counselling on effective malaria chemoprophylaxis and mosquito avoidance measures is essential. There are a limited number of chemoprophylaxis agents approved for use in pregnancy. Chloroquine and hydroxychloroquine are considered safe and are recommended for prophylaxis in pregnant women travelling to areas without chloroquine resistance (McKinney et al., 2020). Mefloquine is the agent of choice for prophylaxis of pregnant women travelling to chloroquine-resistant areas if no contraindications exist (Roggelin & Cramer, 2014). The safety of atovaquone-proguanil during pregnancy has not been established, but small studies have shown no evidence of adverse effects (Roggelin & Cramer, 2014). Primaquine and tafenoquine are contraindicated during pregnancy and breastfeeding because of the risk of glucose-6-phosphate-dehydrogenase (G6PD) deficiency in the foetus (Baird, 2018). Most chemoprophylaxis guidelines advise against the use of doxycycline during pregnancy and breastfeeding (McKinney et al., 2020). Topical mosquito repellents containing DEET are safe and well-tolerated during pregnancy and breastfeeding (Stanczyk et al., 2015).

Older Travellers

Eighty is the new sixty and age is now less of a barrier to international travel than ever before (South African Society of Travel Medicine, South African Geriatrics Society, and International Association for Medical Assistance to Travelers, 2016; Suh & Flaherty, 2019). There is a growing proportion of seniors travelling internationally; an estimated 5–30% of travellers are aged >60 years (European Union, 2020; Gautret et al., 2012; Lee et al., 2017). On cruise ships, up to 37% of passengers are 50–70 years of age and a further 14% over 70 years old (Cruise Lines International Association, 2018). A rapidly increasing interest in the wellbeing of this population is therefore justified.

Definitions as to when one becomes *older* vary from age >50 years as determined by immunologists based on immunosenescence, >60 years as per the World Health Organization (WHO, *elderly individuals*), >65 years according to the cruise industry and others (McClean and the Committee to Advise on Tropical Medicine and Travel [CATMAT], 2011). Some remain fit much longer, such as Yuichiro Miura who climbed Mt Everest a second time aged 80 years and 224 days.

Epidemiological Evidence on Health Problems in Older Travellers

Ageing results in physiological changes including vision and hearing deficits (Torresi et al., 2019), cognitive decline and increased risk of dementia (Jafari et al., 2019). Decreased strength and frailty are associated with susceptibility to falls and an increased risk of fractures due to osteoporosis (King & Lipsky, 2015). Many of those aged 65 years have one or more morbidities (Barnett et al., 2012) and require medication(s), increasing the risk of interactions with medications that may be prescribed for the trip. Reduced functional reserve and homeostatic dysregulation may result in emergencies under extreme conditions (Lee et al., 2017). Immunosenescence is associated with an increased risk of complications with many infections and also with decreased protection by vaccines (Del Giudice et al., 2018; Nichols et al., 2018; Wagner & Weinberger, 2020). The case fatality rate of COVID-19 markedly increases in old patients.

The largest study to evaluate proportionate travel-related morbidity in older versus younger travellers is based on GeoSentinel data (Gautret et al., 2012). These data suggest that older travellers experience higher proportionate morbidity due to more serious diagnoses such as lower respiratory tract infections, cardiovascular and neurologic diseases and injuries, but lower morbidity in relation to diarrhoea and febrile illness (Table 4). Motion sickness is rare among senior citizens.

Older travellers are more likely to need air evacuation while abroad. In one series, over 50% of evacuations were of travellers aged >70 years with trauma and a variety of internal medicine, neurologic and urologic disorders (Sand et al., 2010).

Table 4 Health problems according to age group

Syndrome	18-45 years	≥ 60 years	p-value	Remarks
Respiratory	10.3	14.6	<0.001	Pneumonia, high-altitude pulmonary oedema
Dermatologic	13.3	14.5	0.004	Arthropod bites
Musculoskeletal	3.9	6.5	<0.001	Trauma, injuries
Neurologic	2.2	3.6	<0.001	Vertigo, cerebrovascular accident
Urological	2.8	3.5	0.001	Urinary tract infections
Chronic disease	1.8	3.4	<0.001	Gastro-oesophageal reflux
Cardiovascular	0.5	3.4	<0.001	Heart, phlebitis, pulmonary embolism
Acute diarrhoea	22.9	16.7	<0.001	Bacterial and parasitic
Febrile systemic illness	18.3	12.6	<0.001	Upper respiratory tract infection, influenza/ Influenza-like illness (ILI), dengue, malaria
Chronic diarrhoea	6.5	5.9	0.045	
Psychological	2.1	1.5	0.001	
Oral, dental	2.0	1.1	<0.001	
Obstetric, gynaecologic	2.3	0.3	<0.001	
Genital infections, STD	1.3	0.7	<0.001	

Note: Number of cases (per 100 ill travellers) in ill travellers ($n = 7049$ aged > 60 years, $n = 56{,}042$ aged 18–45 years) seen in GeoSentinel clinics between 1997 and 2008 (Gautret et al., 2012)

Focusing on *vaccine preventable diseases* (VPDs), there are multiple reports on influenza and its complications, particularly during cruise ship voyages (Goeijenbier et al., 2017; Payne et al., 2018). The risk of pneumococcal disease increases with age; observed mainly in association with mass gatherings (Hoang et al., 2019). Based on GeoSentinel data, other VPDs typically affect younger populations, with a median age of <40 years and interquartile range (IQR) with an upper limit <50 years; exceptions include pertussis (median 44 years, IQR 30–61 years) and bacterial meningitis (51 years, IQR 27–60 years) (Boggild et al., 2010).

Older travellers probably do not expose themselves as often to malaria risks compared to younger age cohorts (Gautret et al., 2012), but if they are infected they have a significantly increased risk of severe malaria with acute renal failure and cerebral malaria (Kurth et al., 2017).

From the age of 40 years, risk of VTE is increased (Gavish & Brenner, 2011). The risk of cold stress is highest in the very young and in those aged 60 years or more (Gocotano et al., 2015). Based on experience at the Hajj, heat-related disorders are most prominent in senior pilgrims (Khan et al., 2018). Jet lag is worse in senior travellers (Kim & Duffy, 2018). In contrast to the above, there does not appear to be an association between age and the risk of acute mountain sickness (Gonggalanzi et al., 2016; Wu et al., 2018). Despite increasing achlorhydria there is no increase in the incidence of TD (Torresi et al., 2019).

Travel Health Advice for Senior Travellers

During the COVID-19 pandemic many national authorities advise that older adults abstain from international travel. In some older travellers, fitness to fly (see *Part V Government and Industry Activity: Creating a Safer Journey: Exploring Emerging Innovations in the Aviation Sector*) or to travel at all must be evaluated and discussed.

Older travellers usually make reasonable selections in their destination and know how to avoid excessive stress and physical activity. Many choose organised tours, cruises and all-inclusive resorts rather than individually planned multi-stop journeys. Slightly longer transfer times with options to rest are recommended. Aisle, exit-row or bulkhead seats may be more comfortable and thus advisable for older air or bus passengers. A general check-up, ideally 8 weeks prior to departure, may be indicated before longer or strenuous trips. Additional recommendations relevant for older adults with pre-existing conditions will be discussed below.

With respect to VPDs, the national routine adult immunisation schedule should be completed (Burke & Rowe, 2018; Esposito et al., 2018). Specific travel vaccines may be indicated. For older travellers, influenza vaccination is paramount (Goeijenbier et al., 2017) and vaccination against pneumococcal disease should also be considered. Older travellers undertaking cruise travel or staying in resorts are less likely to be exposed to the risk of rabies (Steffen et al., 2020). Exposure to hepatitis B is also less likely, unless there is a persisting desire for casual sex or the need for medical interventions abroad, which remain unsafe in some (mostly remote) places. The proportion of hepatitis B vaccine non-responders increases with age (Tohme et al., 2011). Older travellers are usually immune to measles, mumps and rubella. Although the risk of hepatitis A is much lower as compared to previous decades (Beaute et al., 2018), there is an elevated case fatality rate of hepatitis A above the age of 65 years. The risk of typhoid is low at most destinations (Greenaway et al., 2014; Muresu et al., 2020; Neumann et al., 2014) and the case fatality rate of typhoid is <1% (Jin et al., 2019). For tick-borne and Japanese encephalitis, the risk of sequelae and death increases with age and those travelling to endemic areas should be offered vaccination (Kaiser & Dobler, 2010). Yellow fever vaccination in older adults is probably more frequently associated with severe adverse reactions, thus this vaccine should only be given if there is a risk of infection, otherwise an exemption certificate will be sufficient (Reno et al., 2020; Teitelbaum et al., 2018).

For prevention of malaria the same fundamental recommendations—personal protection measures (PPM) against mosquito bites and chemoprophylaxis—apply to older and younger travellers (*Part I Health: Travel Medicine and Tourist Health*). Older travellers are typically more adherent to chemoprophylaxis, but less adherent to PPM (Ahluwalia et al., 2020; Del Prete et al., 2019). Older travellers are less likely to experience adverse effects and intolerance to chemoprophylactic medications (Del Prete et al., 2019).

Even though the incidence rate of TD decreases with age (Steffen et al., 2015) it remains a relevant topic and overall the general rules described in *Part I Health: Travel Medicine and Tourist Health* and *Part II Safety: Food Safety and Hygiene*

apply as determined by a consensus conference for prevention and treatment (Riddle et al., 2017). There is some evidence that TD in the elderly may be more serious, for example, dehydration may lead to electrolyte imbalance or increase the risk of cerebrovascular accidents (Yamakawa et al., 2018). Travel kits should be recommended, with particular attention given to options for oral rehydration solutions. For those with a minimally unsteady gait, walking sticks may be useful to reduce the risk of falls and injury.

Conclusions

Healthy older adults can travel to almost any destination reasonably taking into account limitations associated with their age. In preparing for the trip, particular attention should be given to avoid stress and undertake preventive measures against influenza and falls.

Travellers With Pre-Existing Conditions

Pre-existing disease or disability may exist in travellers of any age and require special consideration in pre-travel counselling due to the increased risk of health problems or issues abroad (Wieten et al., 2012). As the risk of a trip may be excessive in the setting of an unstable condition, any chronic illness should be well-controlled prior to travel. Some patients, for example those with chronic arthritis, may experience improvement of their ailment in a warmer climate.

A few rules apply to all conditions. Patients with medication needs should carry at least enough to last for the entire trip. As checked-in luggage may get lost and hand luggage stolen, medication supplies should be split across bags. For some remote destinations, syringes and needles should be packed. Travellers should be advised that it is illegal to import certain medications to some countries (International Narcotics Control Board, 2019). A range of medication interactions with antidiarrhoeals and antimalarials is possible, and practitioners should check for interactions before prescribing these drugs (Baker, 2007; Lee et al., 2017).

In addition to a classical pre-travel consultation, consultation with a specialist regarding the pre-existing disease may be indicated with subsequent discussion between these experts. Patients should carry a detailed report in English or in the language of the destination country prepared by their treating doctor which includes a medication list, recent results and any other relevant information including his/her contact details. Detailed advice for every condition is outside of the scope of this chapter (see Barbeau et al., 2019 for further information).

Cardiovascular Problems

Although cardiovascular events are among the most frequent causes of death abroad and aboard airplanes and other conveyances (Epstein et al., 2019; Lee et al., 2017; Leggat & Wilks, 2009; Stamatakis et al., 2017) underlying cardiovascular conditions rarely preclude travel. Individuals who are able to tolerate vigorous exercise at home will usually manage well during travel and at the destination, unless this is at an exceptionally high altitude. As a rule of thumb, people who are able to climb a flight of stairs without shortness of breath are fit to fly (Hammadah et al., 2017; Smith et al., 2010). Stable coronary heart disease is not a contraindication to travel, but those with unstable disease and/or recent myocardial infarction should be discouraged from travelling due to the stress of travel, exertion of carrying heavy luggage, and abrupt changes in climate that may aggravate their condition.

Patients with stable hypertension can tolerate a prolonged stay abroad or altitude exposure and can be instructed to self-check their blood pressure. Some antihypertensive medications, such as beta-blockers, may interfere with a compensatory increase in heart rate at high elevations. This may result in shortness of breath and symptoms that mimic acute mountain sickness. Antihypertensive or diuretic medication may result in low blood pressure symptoms, with a risk of fainting in zones with a hot climate.

Mild to moderate congestive heart failure usually causes no problems during air travel but may result in progressive problems upon arrival. Patients on diuretics are particularly prone to electrolyte imbalances during bouts of TD or due to excessive perspiration. Altitudes above 2400 meters/8000 feet can also compromise cardiopulmonary function in travellers with pre-existing heart or lung disease or severe anaemia (Donegani et al., 2014).

Patients on medication for arrhythmias and those with prolonged QT requiring malaria chemoprophylaxis need particular attention (Lewis et al., 2020). Those on warfarin should plan monitoring, and those at risk of endocarditis need specialist advice prior to prolonged stays in developing countries. Patients should be safe to travel 10 days after an uncomplicated myocardial infarction and 6 weeks after a complicated event; 2 days after a percutaneous coronary intervention, 14 days after coronary artery bypass grafting, and 1–2 days after insertion of an implantable cardioverter-defibrillator. Patients with older unipolar pacemakers or implanted defibrillators should get clearance from security staff and avoid passing through metal detectors (although theoretically, metal detectors should not induce magnetic interference that results in deprogramming of such instruments).

Long flights or bus, car, and train rides may present a risk of venous (and rarely arterial) thrombosis for patients with risk factors. They must be reminded to maintain adequate fluid intake during the flight, to walk around periodically, and to avoid in-flight sleeping medication. In selected cases, compression stockings, low-dose pre-flight heparin or new oral anticoagulants may be considered; aspirin probably gives insufficient protection (Marques et al., 2018; Ringwald et al., 2014).

With respect to medication, concomitant use of warfarin and doxycycline or atovaquone/proguanil will result in increased anticoagulation. There is no unanimity as to whether intramuscular vaccine injections are contraindicated during anticoagulation (Ringwald et al., 2009; van Aalsburg & van Genderen, 2011). Hydrochlorothiazide may not only result in dehydration but may also increase the risk of non-melanoma skin cancer (Pedersen et al., 2018).

Pulmonary Disease

Patients with pulmonary conditions must be assessed for fitness to fly prior to travel (Lee et al., 2017). Patients with chronic respiratory insufficiency who need oxygen supplementation for long periods on a daily basis are certainly unfit for pleasure travel but, if necessary, may be transported by air (Nicholson & Sznajder, 2014). Patients with chronic obstructive pulmonary disease with acceptable levels of arterial blood gases on the ground may well require oxygen during the flight because oxygen saturation will drop. Arrangements must be made prior to travel with the respective airline.

Chronic obstructive pulmonary disease may be aggravated by high altitude (>2500 m), with patients often suffering from increased dyspnoea. In contrast, patients with asthma may experience easier breathing. Bronchopulmonic disease may be exacerbated, particularly in cities with smog (Vilcassim et al., 2019), whereas chronic bronchitis may improve in a humid, warm climate. Recommendations for the public have been published by the British Lung Foundation (2021). Patients with chronic obstructive airway disease should take ample medication to cope with episodes of aggravation, as required. Immunisation against influenza and pneumococcal disease is particularly important for this at-risk population.

Metabolic and Endocrinologic Disease

Patients with insulin-dependent (type 1) diabetes should avoid travel unless they are stable, able to assess their blood sugar frequently and competently adjust their insulin doses (Wieten et al., 2012). Long-term travellers should ensure that they are free of comorbid complications. The disruption of daily routines and the stress of travel may precipitate episodes of hypo- and hyperglycaemia (Burnett, 2006).

Before travel, patients with diabetes must make sure that they have sufficient stock of the following in their hand luggage (Mullin et al., 2018):

- Insulin (usual supplies, plus extra short-acting insulin)
- Injection equipment
- Blood glucose meter (with extra batteries) and blood glucose testing strips

- Urine ketone and glucose testing strips
- Sugar and snacks for treating hypoglycaemic episodes and in case of meal delays
- Glucagon kit for use in case of hypoglycaemia resulting in unconsciousness (travel companions should be instructed in the signs of hypoglycaemia and use of the kit prior to travel)
- First aid kit
- Diabetes logbook

Diabetic travellers should request special in-flight diets at least 24–48 h in advance. They should take appropriate preventive measures against motion sickness, which may result in hypoglycaemia caused by decreased caloric intake. Selecting appropriate seats in the bus (front), plane (over wing), and on a boat (low, in the centre) may benefit.

Patients with insulin pumps should inform security staff that they should avoid passing through metal detectors (MacNeill & Fredericks, 2015). Although, theoretically, these should not induce magnetic interference resulting in deprogramming of an insulin pump, this cannot be ruled out, particularly in developing countries where the machines may be faulty. Altitude may alter performance of glucometers and insulin pumps (Jendle & Adolfsson, 2011).

Flights crossing no more than three time zones represent no problem to insulin-dependent diabetics, but additional doses of regular insulin may be necessary for longer westbound flights with prolongation of the day. In contrast, for eastbound flights with shorter days, reducing the insulin dose or using short-acting rather than long-acting insulin may be indicated (Chandran & Edelman, 2003; Pinsker et al., 2013). When preparing insulin during a flight, half the normal amount of air should be injected into the bottle due to the decreased air pressure at high altitude. Dehydration resulting from prolonged flights may make glucose control more difficult; therefore, the individual should consume plenty of non-alcoholic fluids, and should frequently monitor blood sugar. Patients should consult their endocrinologist or another competent medical professional for detailed and personalised pre-travel advice. Oral hypoglycaemics for patients with type 2 diabetes can be taken as prescribed, without any adjustments for time zone changes.

The tropics are associated with additional health risks for patients with diabetes. In hot climates, during travel and at the destination, insulin should ideally be refrigerated. However, it will keep for at least 1 month unrefrigerated if protected from freezing or temperatures above 30 °C (86 °F). If insulin is likely to be exposed to heat above 50 °C (approximately 120 °F), protect this with a wide-mouthed thermos or insulated bottle. For trips exceeding 1 month in duration, patients with diabetes should check in advance the local availability and equivalent brand names of their usual form of insulin.

Diabetes increases susceptibility to heat-related problems. Symptoms of hypo- or hyperglycaemia may mimic some of the symptoms of heat exposure, such as weakness, dizziness, headache, and confusion. Increased perspiration may result in an increased risk of cutaneous infection; therefore, hygiene measures should be strictly followed. Diabetic patients with autonomic neuropathy, a condition that

interferes with sweating, should avoid hot climates, or ensure air-conditioned environments are available. Patients with diabetes should be reminded to drink lots of fluids. This is particularly important in senior travellers with type 2 diabetes to avoid dehydration and hyperosmolar coma. Before vigorous exercise, it may be necessary to slightly reduce the dose of insulin.

Diabetic patients must rigorously carry out diabetic foot care and obey common sense rules. They should avoid going barefoot and frequently change their socks to keep the feet dry and comfortable. They must inspect their feet carefully each day and seek immediate medical attention if they detect a foot infection or non-healing cut or puncture wound. If staying in humid climates, an antifungal powder is a useful addition to the first aid kit.

If vomiting occurs and individuals with type 1 diabetes are unable to eat, patients should use insulin (preferably short-acting) at a reduced dose regularly. During any illness, patients should carefully monitor blood sugar levels to accurately determine insulin requirements.

Diabetics should obtain names and addresses of local diabetes associations by consulting appropriate websites. Local diabetic associations can provide information about physicians specialising in diabetes in many parts of the world, as well as restaurants offering special diets, pharmacies open 24 h, and other useful information. The American Diabetes Association provides a wallet-size *Diabetic Alert Card* with emergency information in 13 languages.

Hyperuricaemia may become a problem if recurrent bouts of gout occur. Hyperlipidaemia is of comparatively little relevance with respect to travel.

Renal and Urinary Tract Disorders

Renal insufficiency may be complicated during travel by dehydration due to excessive perspiration or diarrhoea. In addition, serious metabolic problems may occur following dietary errors or diarrhoea, resulting in hyperkalaemia, hyponatraemia, or metabolic acidosis. Finally, uraemia may increase the risk of infection through various mechanisms that decrease immunocompetence. Severe renal insufficiency may be associated with problems in extensive travel or prolonged stays in developing countries. Atovaquone-proguanil is contraindicated for patients with a creatinine clearance <30 L/min (Jolink et al., 2010).

Haemodialysis is available almost anywhere, but it is necessary to organise it in advance (Footman et al., 2015). Various tour operators specialise in tours and cruises for patients on dialysis and kidney-transplant patients, with necessary access to medical resources. The patient may, however, need to be adequately equipped with all the required materials (e.g., erythropoietin), particularly for prolonged stays. Patients must take particular care to avoid infections and to drink enough fluids to avoid thrombosis of their arteriovenous fistula. Dialysis does not affect the metabolism of mefloquine and doxycycline.

Patients with urolithiasis may have an increased risk of recurrence, especially during the first months of stay in a warm climate, thus the need for them to drink plenty of fluids. A pre-departure ultrasonic evaluation may occasionally be indicated. Prostatic hypertrophy and other conditions resulting in urinary urgency may present a challenge in transit, particularly on planes and buses.

Men with benign prostatic hyperplasia should avoid decongestants and antihistamines in the setting of coryzal symptoms as these may lead to urinary retention. They should carry a nightlight or torch to safely find the bathroom in the dark and should be encouraged to select aisle seats.

Disorders of the Gastrointestinal Tract

Chronic inflammatory bowel disease may predispose travellers to enteric complications if they are staying in areas with high risk of gastrointestinal infection or at high altitude (Chan et al., 2018; Vavricka et al., 2014). Patients with colostomies planning to fly should use large bags as air expansion may result in increased output. Chronic liver disease is a concern because of the risk of hepatic infections resulting in deterioration of the condition. Patients with chronic hepatitis B should be immunised against hepatitis A and avoid travelling to those countries where hepatitis E is hyperendemic.

Patients on aspirin, or those using non-steroidal anti-inflammatory products must be aware of the risk of gastric mucosal injury and the risk of bleeding. Concerns that proton pump inhibitors or other contributors to a reduced gastric acid barrier may increase the risk of TD are justified (Bavishi & Dupont, 2011; Wieten et al., 2012). Patients with diverticulosis should carry antibiotics to treat a bout of diverticulitis and should abstain from antimotility agents in the event of diarrhoea. Haemorrhoids may flare up after prolonged sitting, excessive alcohol intake, or consumption of spicy food. In these patients, the travel medical kit should contain the necessary medications. Participants on expeditions traveling to remote areas may consider elective surgical care to prevent potential problems (e.g., appendicitis).

Dermatological Problems

Sunlight, heat, moisture, cold dry climate, and positive or negative emotions may aggravate or alleviate some skin diseases. A few people have a genetically determined higher susceptibility to photosensitivity. Patients who take oral retinoids or doxycycline should be warned of sunburn. Sunlight (more specifically, ultraviolet light) may provoke symptomatic herpes simplex infection and may also aggravate seborrheic dermatitis, rosacea, Mallorca acne (acne aestivalis), and transient acantholytic dermatosis. Ultraviolet (UV) radiation may also result in skin cancer, particularly in ageing skin or those using hydrochlorothiazide medication (Daniels

et al., 2020). In contrast, psoriasis is usually improved by UV light, but sunburn of the untanned skin may cause Koebner's phenomenon and lead to exacerbation. UV light induces peeling of the skin and usually improves acne vulgaris. Some forms of urticaria may improve during a vacation with greater exposure to sunlight.

Many agents used for malaria prophylaxis (atovaquone/proguanil, chloroquine, doxycycline, mefloquine, sulfadoxine/pyrimethamine) may be associated with exacerbation of psoriasis or may result in phototoxicity; additionally, sulfadoxine/pyrimethamine may cause severe cutaneous adverse reactions (Amelot et al., 2014; Goetze et al., 2017; Nunes et al., 2017).

Heat plays a prominent role in intertrigo and hyperhidrosis. Individuals with anhidrotic ectodermal dysplasia have no eccrine sweat glands and experience heat congestion when they are exposed to sun and heat. Travel to tropical countries may be life-threatening. Cold will aggravate Raynaud's disease and syndrome, peripheral vascular malperfusion, vasculitis owing to cryoglobulins and cryofibrinogens, erythrocyanosis crurum, acrocyanosis, and cold panniculitis.

A dry climate may exacerbate ichthyosis vulgaris and atopic dermatitis. Individuals with dry skin should use a body lotion after a shower, take brief showers, and use soap only on the intertriginous areas.

Allergies

Travellers prone to allergies should avoid known allergens, but they face the risk of being exposed to new ones during travel. Air pollution is associated with atopic dermatitis (Baek et al., 2020). House dust mites thrive in tropical conditions and can be particularly sensitising. The risk of seasonal reactions to pollens varies region by region. Food allergies are a constant threat due to unknown ingredients in exotic dishes. Various insect bites may result in anaphylaxis. Some medications recommended for use during travel in tropical areas may trigger hypersensitivity reactions. Avoidance of allergens is more difficult in a foreign environment.

Travellers with allergies should carry identification cards that include a list of substances to which they are allergic and carry a travel medical kit containing antihistamines or corticosteroids.

Other Pre-existing Health Problems

Degenerative rheumatologic disease is often improved during a stay in a warm climate. Depending on the type of aircraft seat, low back pain could often be aggravated during and after a long flight; thus arranging for stopovers during long journeys and spending a night in bed may help.

Among neurologic disorders, epilepsy is frequently observed in-flight or upon arrival; often this is associated with drugs or non-adherence to medication

(Alonso-Canovas et al., 2011). Mefloquine and chloroquine may lead to a recurrence of seizures (Schneider et al., 2013). Tension headaches may improve while abroad because the individual is removed from the usual factors causing stress.

Psychological and psychiatric conditions are a frequent reason for air evacuation, primarily in expatriates (Gardiner et al., 2020; Linton & Warner, 2000). Mefloquine is contraindicated in individuals with a history of such conditions. Patients with a history of substance abuse and individuals who cannot easily adapt to new conditions are not good candidates for a prolonged stay abroad (Foyle et al., 1998). Some people may become disoriented in a strange town. It may help them to carry a card with the name, address, and telephone number of their residence, as well as a card showing their destination to obtain directions or assistance if they get lost (Bauer, 2019).

Physically Challenged Travellers

The benefits of travel are increasingly available to people with physical limitations, as globally there is an increased awareness and support for their needs. Specialised organisations, tour operators, air- and cruise lines and hotels offer advice and support tailored for particular disabilities, but this must be requested in advance (Bauer, 2018; Jorge et al., 2005).

Wheelchair users are usually advised that a lightweight folding chair is most convenient during travel. It is useful to carry the necessary tools for repairs as well; power wheelchairs may be too complex for the available infrastructure in lower income countries. Rental may be possible at some destinations. Many cities throughout the world publish accessibility handbooks, and local tourist bureaus will provide information.

For the visually impaired, transport of guide dogs across international borders can be a major problem, as quarantine may be imposed. Entry regulations for the destination and regulations for re-entry into the country of origin should be evaluated pre-travel. Additional vaccinations may be requested.

Hearing-impaired travellers should inform transportation and hotel staff of their impairment so that they do not miss travel announcements or emergency information and alarms. Those with hearing aids must carry sufficient supply of batteries.

The Immunocompromised Traveller

The immunocompromised are a heterogenous but increasingly important group of travellers who may present to any travel health practitioner (Patel et al., 2015). The term *immunocompromised* encompasses a range of hosts with varying degrees of immune dysfunction, including transplant recipients, cancer patients, patients receiving immunomodulatory treatments, HIV-infected, and asplenic individuals.

Immunocompromised travellers often travel to *high-risk* destinations and appear just as likely to engage in risky behaviours as healthy travellers (Bialy et al., 2015; Schwartz et al., 2015). They are often at increased risk for acquisition and severity of travel-related infections, but risks vary according to the intensity of the underlying immune dysfunction, travel destination and activities (Aung et al., 2015). There is also the potential risk of a flare or complications related to their underlying disease during travel. Vaccine choices, timing and responses are highly dependent on the underlying cause and degree of immunosuppression; live vaccinations are frequently contraindicated, and vaccine responses may be suboptimal (Rubin et al., 2014). Drug interactions between immunosuppressive medications and commonly prescribed travel drugs may occur (Kotton et al., 2013).

While special considerations exist for immunocompromised travellers when it comes to pre-travel counselling and preparation, most travel can be undertaken safely and there are few absolute contraindications to travel. Detailed advice for every immunocompromised patient group is outside of the scope of this chapter; see Bourque et al., 2019; Kanhutu et al., 2017; Kotton et al., 2019; Rubin et al., 2014; Torresi et al., 2019 for further information. The following recommendations apply to all immunocompromised groups. Pre-travel preparation can be optimised by beginning the risk assessment process early, communicating risks effectively, and vaccinating prior to immunosuppression or after immunological recovery where possible. Patients taking medications should carry enough medication to last the trip, plus some extra, and a detailed medical letter outlining their current immune function, health status, medication list and treating doctor's contact details. All immunocompromised travellers should be informed about how to prevent and manage the more common infections that they may encounter, and when to seek medical attention. Unvaccinated travellers with severe immunocompromise should be strongly discouraged from travel to destinations with true risk of yellow fever (Freedman & Chen, 2019).

Epidemiological Evidence for Health Problems in Immunocompromised Travellers

While few studies have evaluated the incidence of health problems encountered by immunocompromised travellers, they appear to be at higher risk for serious health problems during or after travel compared to their immunocompetent counterparts, with high rates of hospitalisation when illness occurs (Dekkiche et al., 2016; Roukens et al., 2007; Wieten et al., 2012). They may be more susceptible to a range of bacterial, fungal, viral and parasitic infections, although the infections that pose an increased risk and the degree of susceptibility vary according to the extent and nature of immune dysfunction (Aung et al., 2015; Kotton, 2012). The risk of TD may be increased (due to reduced mucosal immunity and/or proton pump inhibitor

therapy) and disease may be more severe (Suryapranata et al., 2019; van Aalst et al., 2018).

Food- and water-borne parasitic infections that are typically self-limited in immunocompetent patients (e.g., cryptosporidiosis, giardiasis and cyclosporiasis) may cause prolonged severe diarrhoea in the immunocompromised (Ericsson et al., 2001). Similarly, bacterial infections (such as non-typhoidal salmonellosis and shigellosis) may be complicated by bacteraemia, invasive disease and recurrence (Gordon, 2008). Following exposure to tuberculosis (TB), risk of progression to active disease is increased; this is especially true for HIV-infected individuals and those receiving anti-TNF-alpha inhibitor therapy (up to 10-fold increased risk) (Denholm & Thevarajan, 2016). Endemic fungal infections posing an increased risk of severe outcomes for the immunocompromised (particularly HIV-infected individuals and transplant recipients) include talaromycosis (formerly penicilliosis) in Asia, coccidioidomycosis and paracoccidioidomycosis in the Americas, and histoplasmosis and blastomycosis (distributed worldwide, but endemic in North America) (Cao et al., 2019; Lee & Lau, 2017; Miller et al., 2013; Panackal et al., 2002). Risk of complications from influenza infection is increased in transplant recipients, cancer patients, and those receiving some biologic therapies; additionally, influenza vaccine immunogenicity in these populations is typically low (Bosaeed & Kumar, 2018). Immunosuppression is a well-established risk factor for development of disease following *Leishmania* exposure, and immunocompromised individuals are more likely to develop diffuse and disseminated forms and experience disease reactivation (van Griensven et al., 2014).

COVID-19 in the Immunocompromised

Published data relating to the incidence and severity of COVID-19 in immunocompromised individuals are still limited, but organ transplant and cancer patients appear to be more likely to need intensive care and more likely to die than the general population (Fung & Babik, 2020; Belsky et al. 2021). Amongst solid organ transplant recipients, increased COVID-19 disease severity and mortality has been reported, with comorbidities highly prevalent among those infected (Cravedi et al., 2020; Fraser et al., 2020; Hoek et al., 2020; Pereira et al., 2020). Higher rates of hospitalisation and higher case fatality rates have been reported amongst cancer patients in cohort and registry studies (Kuderer et al., 2020; Lee et al., 2020). Subgroups at increased risk of worse outcomes (e.g., severe disease and death) appear to include those with lung cancer, haematological malignancies, and recent active therapy (Kuderer et al., 2020; Liang et al., 2020; Mehta et al., 2020; Yang et al., 2020; Yu et al., 2020). The risk of COVID-19 acquisition may be increased in cancer patients, with these individuals making up a larger proportion of COVID-19 cases in both the USA and China compared to the general population (Liang et al., 2020; Miyashita et al., 2020). People living with HIV also appear to be at increased risk of severe COVID-19 disease and mortality (Bhaskaran et al., 2021; Tesoriero

et al., 2021). Existing data do not show an increased risk of severe COVID-19 in patients taking biologic therapies or targeted disease-modifying anti-rheumatic drugs (DMARDs) (Brenner et al., 2020; Fung & Babik, 2020).

Patients Receiving Immunosuppressive Medications

Indications for immunosuppressive medications are varied, and include autoimmune diseases, malignancies, and transplantation. Classic immunosuppressive drugs include corticosteroids, antimetabolites (e.g., azathioprine, methotrexate), calcineurin inhibitors (e.g., cyclosporine, tacrolimus) and cancer chemotherapeutic agents (Askling & Dalm, 2014; Zwar, 2020). In recent decades, there has been a dramatic increase in the availability and use of *biologic* agents (drugs derived from living organisms or their products), many of which have immunosuppressive or immunomodulatory properties (Askling & Dalm, 2014; Hall et al., 2018). Immunosuppressive medications may be administered alone or in combination, and the potential travel-related infection risks are dependent on the dosage(s) and mode(s) of action of the agent(s) received (Hall et al., 2018). Live vaccinations are contraindicated in most patients receiving immunosuppressive medications, and responses to inactivated vaccines may be blunted (Rubin et al., 2014).

High-dose corticosteroids, generally defined as doses >20 mg/day of prednisolone or equivalent for ≥2 weeks, are well-recognised to be associated with an increased risk of severe infections (Youssef et al., 2016). Live vaccines should not be administered until at least 1 month after cessation of high-dose corticosteroids (Australian Technical Advisory Group on Immunisation, 2018). Treatment with tumour necrosis factor (TNF)-alpha inhibitors is associated with increased susceptibility to granulomatous and intracellular infections, such as TB (Hall et al., 2018). Given the increased risk of progression to active TB following TB exposure in those receiving TNF-alpha inhibitors; pre- and post-travel screening for TB should be considered for travellers to high incidence countries, particularly those planning extended stays (Denholm & Thevarajan, 2016). A detailed description of the potential travel-related infection risks and pre-travel recommendations for every immunosuppressive agent is outside of the scope of this chapter, but readers are encouraged to seek further detail (see Australian Technical Advisory Group on Immunisation, 2018; Hall et al., 2018; Kotton et al., 2019).

Transplant Recipients

Transplant recipients include those with solid organ transplants (SOT) and haematopoietic stem cell transplants (HSCT). The degree of immunosuppression in HSCT recipients is dependent on the conditioning agents administered pre-transplant, and whether the transplant is derived from the patient's own (autologous) or donor

(allogeneic) stem cells (Aung et al., 2015). Most HSCT recipients undergo an initial period of intense immunosuppression, with impaired immunity and functional asplenia, but recover their immune function over time, to the point where they may be presumed immunocompetent at or beyond 24 months post-transplant provided they do not develop graft-versus-host disease (GVHD) requiring treatment (Aung et al., 2015; Rubin et al., 2014). In contrast, most SOT recipients undergo an initial period of moderate immunosuppression (usually greatest in the first 6 months post-transplant) but are committed to long-term immunosuppression with anti-rejection drugs (Aung et al., 2015).

Transplant recipients should be encouraged to avoid high-risk travel during periods of intense immunosuppression (e.g., in the 6–12 months post-transplant or during episodes of rejection or GVHD) (Aung et al., 2015). Live vaccines should not be administered to SOT recipients or to HSCT recipients within 24 months of transplantation (Rubin et al., 2014). Inactivated vaccines are usually considered safe, but antibody responses may be blunted and additional or booster doses may be required to achieve adequate responses (Trubiano et al., 2016). Routine vaccinations should be up-to-date pre-travel. Potential drug-drug interactions should be reviewed prior to prescribing travel-related medications such as malaria chemoprophylaxis (Kotton et al., 2013; Trofe-Clark et al., 2013). As transplant recipients may be at increased risk of TD-related complications (including bloodstream infection) and diarrhoea-related dehydration may result in renal insufficiency and anti-rejection drug toxicity, TD should be managed aggressively (Beeching et al., 2018). Early, aggressive fluid and electrolyte replacement is recommended, along with empiric antibiotic therapy for those with fever, bloody stools, or three or more episodes in one day (Beeching et al., 2018). Sun protection should be recommended due to the increased risk of skin cancer in transplant patients receiving immunosuppressive medications (Kotton et al., 2013). Transplant recipients should also be advised to avoid caving, spelunking, and dust-laden activities and environments (e.g., construction, demolition and excavation sites) due to the risk of inhalation of fungal spores (Miller et al., 2013; Panackal et al., 2002).

HIV-Infected Travellers

The advent of highly effective combination anti-retroviral therapy (ART) has led to dramatic improvements in the health of HIV-infected individuals, and those who adhere to their treatment regimens can now expect a near-normal life expectancy (Fauci & Lane, 2020). However, HIV-infected individuals may be at increased risk for travel-related infections and adverse outcomes, with the greatest risks seen in those not on ART or with lower CD4+ T-cell lymphocyte counts (Bourque et al., 2019).

HIV-infected travellers should be advised to adhere to food and water precautions, safe sex practices, and insect bite avoidance during travel (Bourque et al., 2019). As HIV infection is an independent risk factor for VTE (Bibas et al., 2011)

they should be encouraged to mobilise frequently and stay well-hydrated while in transit (especially on long flights) (Bourque et al., 2019). Most vaccines are safe in HIV-infected individuals, but live vaccines should be avoided in those with CD4+ counts <200 cells/mm^3 (Rubin et al., 2014). Because HIV-infected individuals may have blunted post-vaccination immune responses and shorter durations of seroprotection, additional or booster doses of some vaccines may be recommended. For example, a booster dose of yellow fever vaccine is recommended for HIV-infected travellers travelling to areas with yellow fever risk if it has been more than 10 years since their last dose and they have a CD4+ count of 200 ≥ cells/mm^3 (Staples et al., 2010).

Practitioners should consult current guidelines for HIV-specific vaccine recommendations (Crum-Cianflone & Sullivan, 2017a, 2017b). Potential drug-drug interactions should be reviewed prior to prescribing travel-related medications such as malaria chemoprophylaxis; an excellent free HIV drug interaction checker is available at the University of Liverpool's website (HIV Drug Interactions, 2021). Due to increased risk of progression to active TB following TB exposure, pre- and post-travel screening for TB should be considered for HIV-infected individuals travelling to high incidence countries, particularly those planning extended stays (Denholm & Thevarajan, 2016). HIV-infected travellers should be aware that some countries have laws that may restrict entry for individuals with HIV, and be advised to speak with the destination country's consulate or embassy prior to travel (Bourque et al., 2019).

Asplenic and Hyposplenic Travellers

Asplenic and hyposplenic individuals are at increased risk for severe infection due to encapsulated bacteria (e.g., *Streptococcus pneumoniae* and *Neisseria meningitidis*), bacteria transmitted through animal bites (especially *Capnocytophaga canimorsus*) and intra-erythrocytic parasites such as malaria and babesiosis (Chotivanich et al., 2002; Luu et al., 2019; Rosner et al., 1984). Pre-travel education is of vital importance; individuals should be aware of the need to seek medical attention in the event of a fever or animal bite and should carry an emergency supply of antibiotics (Boeddha et al., 2012; Kanhutu et al., 2017). Those who are not otherwise taking antibiotic prophylaxis should be encouraged to do so during periods of travel. Patients travelling to malaria-endemic areas should be aware of the risk of severe malaria and take optimal precautions to prevent infection (mosquito avoidance measures plus antimalarial chemoprophylaxis) (Kanhutu et al., 2017). Asplenia is not a contraindication to vaccination and live vaccines pose no risk to asplenic and hyposplenic individuals (Rubin et al., 2014). In addition to recommending appropriate travel vaccines, practitioners should ensure that routine vaccinations are up-to-date, including specific vaccines recommended for asplenic and hyposplenic individuals (annual influenza vaccine, pneumococcal [both conjugate and

polysaccharide vaccines], meningococcal [ACWY and B] and Hib vaccines, Kanhutu et al., 2017; Rubin et al., 2014).

Travel in Those Who Have Recovered From COVID-19

Increasingly, patients who have recovered from COVID-19 will wish to travel. Emerging literature suggests that COVID-19 infection may result in long-term sequelae, but further research to characterise the frequency and extent of sequelae is needed (Yelin et al., 2020; Zhao et al., 2020). The degree to which individuals develop protective immunity following infection remains unclear, and cases of reinfection have been reported (Tillett et al., 2020; To et al., 2020). Optimal pre-travel advice for individuals who have recovered from COVID-19 and are planning to travel is yet to be established, but considerations may include assessment for sequelae (e.g., pulmonary function testing), assessment of exposure risk at the destination, and advice on preventive measures such as hand hygiene and vaccination.

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