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Review

Travelling with cystic fibrosis: Recommendations for patients and care team members☆

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Abstract

There are no European Guidelines on issues specifically related to travel for people with cystic fibrosis (CF). The contributors to these recommendations included 30 members of the ECORN-CF project. The document is endorsed by the European Cystic Fibrosis Society and sponsored by the Executive Agency of Health and Consumers of the European Union and the Christiane Herzog Foundation.

The main goal of this paper is to provide patient-oriented advice that complements medical aspects by offering practical suggestions for all aspects involved in planning and taking a trip. The report consists of three main sections, preparation for travel, important considerations during

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travel and at the destination, and issues specific to immunocompromised travellers. People with CF should be encouraged to consult with their CF centre prior to travel to another country. The CF centre can advise on the necessary preparation for travel, the need for vaccinations, essential medications that should be brought on the trip and also provide information relating to CF care in the region and plan of action in case of an emergency.

Keywords: Cystic fibrosis; Travelling; Holidays; Vacation

Contents

1. Introduction

The increased life expectancy and improved quality of life over the past three decades enable people with CF to participate in every aspect of modern life, including tourism. The wish to travel should be respected and supported depending on the patient's state of health. The risks related to travel can be higher for persons with CF than for healthy people. This may be most challenging if the individual is travelling in a country without specialized CF care. Detailed preparation along with prior medical screening and advice is important to assure safe and comfortable travel. CF caregivers are increasingly confronted with travel-related questions from CF patients, a fact that is also reflected in the growing number of inquiries about this issue to the web-based ECORN-CF expert advice (www.ecorn-cf.eu).

Several guidelines have been written to assist CF caregivers in the evaluation and monitoring of patients and the prevention of clinical deterioration (available at www.ecfs.eu) [1–8].

However, there are no European recommendations on issues specifically related to travel.

The aim of this document is to provide guidance for travel for people with CF and to assist them to responsibly plan the stay abroad. We hope that these recommendations will be adopted by all European CF centres to provide a basis for improved patient care. It may be necessary to specifically train the care team members in giving educated advice for travel related questions based on the information given in this overview.

1.1. Methodology

Within the international expert advice system of the ECORN-CF project, many questions from patients and care team members were asked related to the topic "travelling with CF" and it proved to be difficult to assess the quality of answers since no commonly accepted guideline on this topic was available. Therefore this topic was chosen as a "consensus statement" theme by the ECORN-CF study group. Following a systematic review of the literature (search terms: CF AND/OR chronic lung disease AND travelling AND/OR vacation AND/OR holiday AND/OR sports), subtopic-specific working groups developed first drafts of manuscript modules. These drafts were then further developed according to a modified (simplified to two iterations) Delphi procedure among all authors listed. If evidence was lacking and in all situations where unanimous consensus could not be reached, agreement among the authors was achieved during consensus conferences which took place in Frankfurt, Germany (November 5, 2008) and Prague, Czech Republic (October 6 and 7, 2009), involving all members of the ECORN study group.

2. Preparation before travelling

2.1. Medical assessment and counselling

In preparation for their stay abroad, patients need to be aware that a CF centre might not always be close by, which can be crucial in case their condition is deteriorating. If trouble develops during the trip, individuals with CF should contact their home CF centre initially.

CF centres should provide a thorough pre-holiday/pre-travel medical assessment for each patient before agreeing that they are fit to travel. There are few absolute contra-indications for travel, but it is advisable that CF individuals consider how travel will impact them and prepare appropriately. Prior to departure, clinical status should be optimized. Some patients achieve this with intensive treatment with intravenous antibiotics for two/three weeks prior to travelling.

Patients may travel to different climates and the associated risks of dehydration may be most prominent for individuals with CF but exposure to high ozone concentrations, pollutants, infectious agents (via air, food, and poor hygiene) may be greater in a person with a chronic disease such as CF.

There are logistic issues to consider as well, such as availability of time, space and equipment for therapy, appropriate storage of drugs, and access to medical care. Travel may bring about fatigue, stress, and motion sickness. Patients may engage in activities different from their usual ones. Occasionally, caregivers have to advise that a person with CF is medically unfit to travel and to refuse to sign insurance forms. Unless the trip is to access medical treatment, patients with an unstable condition such as acute pulmonary exacerbation, haemoptysis, gastrointestinal obstruction, or uncontrolled diabetes should postpone their travel until their medical condition has stabilised.

- People with CF need to be well prepared for travel and should consult their CF centre team when considering a trip in another country.
- If trouble develops during the trip, individuals with CF should contact their home CF centre initially.

2.2. Air travel and staying at high altitude

Air travel and/or staying at high altitude need to be highlighted because these conditions expose the individual to a lower atmospheric pressure (see table "Correlation between altitude, air pressure and oxygen content" at http://ecorn-cf.eu/index.php?id=265&L=8). The partial pressure of oxygen is inversely proportional to the altitude, hence, alveolar partial pressure falls with increasing altitude, causing patients to be more at risk of serious desaturation and hypoxaemia. In patients with more severe lung disease, air travel or a stay at high altitude may lead to hypoxia below a PaO_2 of 6,6kPa (50 mmHg), which is considered a significant threshold [9].

Commercial aircraft operate at different cabin altitudes and pressures ranging from 300 m (1000 ft) to 3000 m (10,000 ft). The Joint Aviation Authority has restricted the mean cabin altitude to 2438 m (8000 ft). This will affect the inspired oxygen available in the cabin, which ranges from 14.7% to 16.8%, depending on the airline and aircraft (compared to 21% at sea level). The current guidelines of the American Thoracic Society (ATS) and British Thoracic Society (BTS) recommend that an arterial oxygen tension (PaO_2) of >6.6k Pa (50 mm Hg) be maintained during flight in patients with chronic lung disease [10,11].

The effects of short episodes of hypoxemia in subjects adapted to chronic hypoxemia are unclear. It was shown that people with CF can tolerate PaO_2 values below 6.6kPa (50 mm Hg) for several hours without cardiac decompensation or cerebral symptoms, which suggests that BTS guidelines may not be fully applicable in these patients. It can be assumed that CF patients are adapted to intermittent severe hypoxia, especially during exercise [12]. It is noteworthy that individuals with CF usually carry no cardiovascular risk and are, on average, younger than patients with chronic obstructive pulmonary disease. Indeed, just considering a PaO_2 cut-off for requiring supplemental oxygen during a flight is an 'oversimplification'. Ideally one should take into account the degree of hyperventilation that the patient will be able to sustain as well as

his haemoglobin value, cardiac output and other factors that co-determine oxygen delivery to the tissues. Special attention has to be paid to patients with severe bronchial collapse or obstruction, since they may not be able to compensate for hypoxia by hyperventilation [12]. Patients with liver cirrhosis and oesophageal varices may be at higher risk for bleeding during extended flights or stay at high altitude [13].

Absolute contra-indications for air travel—unless it is a medical transport for life-saving procedures—could include: severe respiratory insufficiency, right heart failure or hemodynamic instability. Patients with a previous pneumothorax should wait for 6 weeks after definitive surgical intervention [11].

- For CF patients, duration of flight and patient condition are the main predictors of medical safety during air travel.
- All people with CF should discuss air travel with their CF doctor.

2.3. Predicting hypoxia at altitude

Most data on flight associated hypoxia are not derived from studies in CF individuals but have been extrapolated from other chronic obstructive lung diseases. In the past, several tests to measure patients' flight eligibility have been developed and evaluated [14–23]. Currently, exposure to a hypobaric chamber or hypoxic challenge at low altitude is used to mimic in-flight conditions [12,24]. The tests should be performed when the patient is clinically stable and relatively close to (not earlier than three months before) the planned travel.

Exposure to a hypobaric chamber provides good simulation of in-flight conditions; however, it is not always readily available, not tolerated by all patients and expensive. The Aerospace Medical Association and the British Thoracic Society recommend the hypoxia inhalation test (HIT), which involves breathing a hypoxic gas mixture (15% oxygen in a nitrogen balance) for 20 min with the aim of predicting hypoxemia at the maximum allowable cabin pressure altitude of 2438 m (8000 ft) [11,25]. In-flight oxygen therapy is recommended if the HIT PaO_2 falls below 6.6–7.4 kPa (50–55 mmHg) [26] (see table "Simulated altitudes by different FiO_2" at http://ecorn-cf.eu/index.php?id=265&L=8).

Several authors have shown that both hypobaric chamber and HIT are safe and predict PaO_2 at altitude of patients with obstructive lung disease accurately [17,27]. However, both tests are performed in a stable environment and may not fully represent the physical stress and environmental variability of air travel, particularly over longer flights [17,28–31]. The addition of a 50 m walk test during the HIT significantly worsened hypoxemia in patients with respiratory diseases [32]. On the other hand, the majority of patients who would have qualified for the use of in-flight oxygen following HIT travelled safely without additional oxygen [24,26,33]. Therefore, a HIT PaO_2 <7.4 kPa (55 mm Hg) does not automatically indicate the need for in-flight oxygen therapy. Rather, it should prompt an informed discussion between the patient and clinician about the benefits and risks of flying with or without supplemental oxygen (Table 1). Recently, it was reported that patients with an FEV1 persistently above 55% predicted are very unlikely to have significant desaturation during air travel [24,34]. However, if flight eligibility of patients is in doubt, the tests described above should be performed. If those tests are not available (e.g. due to geography and resource issues), it is recommended to prescribe oxygen during flight for patients at possible risk of desaturation.

Further research is required to determine how the degree and duration of hypobaric hypoxia will influence the relative risk of adverse events in CF patients.

- Prediction of in-flight oxygen may be helpful especially in individuals with CF who have severe lung disease, co-morbidity with other conditions worsened by hypoxemia, pre-existing requirement for oxygen, or a history of air travel intolerance.

2.4. Air travel and oxygen supplementation

2.4.1. Prior to departure

Airlines usually require the patient to carry a prescription for oxygen at all times. Many have their own airline-specific medical form the doctor must complete. These are usually valid for one year and should include information on the passengers' fitness to travel and his/her ability to operate the oxygenation device and respond appropriately to its alarms. The phases of the flight during which oxygen is medically necessary (taxi, takeoff, cruise, and landing) should be specified. Since many carriers charge a fee for supplemental oxygen, the insurance provider of the individual with CF should be contacted in advance to determine coverage for oxygen needs while travelling. Furthermore, the patient must contact the local providers for oxygen use during any stopover(s) and at the final destination. This contact can usually be set up by the oxygen provider in the home country.

Table 1
Factors to consider when recommending supplemental oxygen.

Medical history
Stability of pulmonary disease
Previous experiences (symptomatic on previous holidays)
Duration of flight
Duration of holiday
Destination, altitude, activity
Physical examination
Lung function tests
Blood gas analysis
Arterial oxygen saturation
Results of hypoxic challenge test

2.4.2. Assistance at the airport

According to recent EU rules, people with reduced mobility should have the same access to air travel as other passengers (EU regulation no. 1107/2006). Under anti-discrimination legislation, airlines and tour operators are forbidden to refuse passengers service on the basis of reduced mobility unless "duly justified" by safety reasons. Therefore, since 2008, disabled people are entitled to receive free-of-charge assistance in all European airports as well as on board planes taking off in the EU. Travellers should inquire with their airline prior to departure which services they offer free of charge. The list of responsibilities for airports and airlines—for which they will have to bear costs—includes providing the relevant infrastructure for disabled passengers as well as carriage for wheelchairs and medically necessary equipment. Some airlines offer special ground services such as separate check-in, priority boarding, etc. Travellers with limited mobility should contact the airline at least 48 h prior to departure about any assistance necessary, which will then be arranged by the airport personnel.

2.4.3. Oxygen supplementation during air travel

For travellers who require in-flight supplemental oxygen, each airline has its own policy for on-board oxygen transport and in-flight oxygen usage (for comprehensive information see http://www.european-lung-foundation.org). It is recommended that the airline should be notified at the time reservations are made and again 48 h before flight time that the patient intends to travel with oxygen.

If therapeutic oxygen is required for use during the flight there are several options. By international law, liquid oxygen is not permitted on board any aircraft. Most European airlines allow passengers to carry and use a small gaseous oxygen cylinder of not more than 2 l capacity (UN-1072, 200 bar). However, this service is prohibited on flights to/from/via the USA, Canada and Mexico. The oxygen cylinder must be stowed in a solid case under the front seat during flight, if possible also during usage. Some airlines will allow empty oxygen equipment to be stowed in the baggage, but it must be verified as empty and the regulator removed. It is important to check with the airline ahead of time if they will allow empty systems/tanks as stowed or checked baggage.

Most airlines provide oxygen on board their aircraft at an additional cost depending on the routing (continental or intercontinental flights). A separate charge usually applies for each flight. The method of oxygen delivery (continuous, demand system) and maximum flow rate vary between airlines and might be limited. The newest portable equipment available for oxygen users are Portable Oxygen Concentrators (POCs). These units are lightweight and can run on electrical or battery power. Since May 2009, POCs are allowed on all flights originating or ending in the United States. A limited number of POCs have been approved by the Department of Transportation for use during air travel (9/2009: Inogen One, AirSep Lifestyle, AirSep Freestyle, SeQual Eclipse and Respironics EverGO). The POC will need sufficient battery power to cover pre-flight, in-flight and post-flight time, including potential delays.

- If a person with CF needs in-flight oxygen (such as all persons on long-term oxygen therapy [LTOT]), the airline should be informed beforehand.

2.5. Prevention of travel related infection

Routine hygienic precautions have to be followed carefully and hydroalcoholic solutions for hand disinfection should be carried and used. Each traveller should be up to date with their routine vaccinations according to age, as recommended by the national vaccination schedule. Moreover, additional vaccinations and safety measures may be recommended for international travel, depending on the destination (Table 2).

2.5.1. General considerations on routine vaccinations in CF

National recommendations and strategies of immunisation should be applied to all subjects including those with CF. However, individuals with CF may have easily escaped normal national immunisation programs, being absent from school and admitted to the hospital for treatment in the past and so run a higher risk of incomplete and delayed immunisation than healthy children [5,35].

Before travelling, a vaccination review should be done, and any gaps in the vaccination schedule should be remedied by catch-up. Specific antibody monitoring is helpful in determining the

Table 2
Recommended vaccines for travellers [5].

Routine vaccinations	Diphtheria, tetanus, pertussis
	Diphtheria, tetanus, pertussis adolescent booster[a]
	Hepatitis B[a]
	Haemophilus influenzae type B
	Human papillomavirus (HPV)[a]
	Influenza[b]
	Measles, mumps, rubella
	Pneumococcal disease[a]
	Poliomyelitis
	Rotavirus[a]
	Tuberculosis (BCG)[c]
	Varicella[a]
Selective use for travellers	Hepatitis A[b/d]
	Typhoid fever
	Yellow fever[d]
	Cholera
	Japanese encephalitis[d]
	Tick-borne encephalitis
	Meningococcal ACWY[d]
	Rabies
Mandatory vaccinations for some countries	Yellow fever[d]
	Meningococcal ACWY[d]
	Poliomyelitis

[a] Vaccines being currently introduced in some countries.
[b] Routine for certain risk groups, selective for travellers.
[c] No longer routine in most industrialised countries.
[d] Not included in the routine immunisation program in most countries.

need for individual boosters [5,36]. With regard to BCG, national guidelines should be followed. Tuberculosis is not frequently a problem in CF patients, but diagnosis is obvious. Since occult TB could be reactivated after transplantation, immunisation in accord with established local practice seems logical [5].

2.5.2. Specific travel vaccines

Influenza vaccine: recommended annually for all CF patients aged 6 months and older. This should also be applied to travellers (typically November–February in the Northern Hemisphere, April–September in the Southern Hemisphere and throughout the year in the tropics).

Inactivated hepatitis A vaccine and recombinant hepatitis B vaccine: this has been shown to be safe and efficacious in preventing infection [37]. Most adult CF patients might not have been vaccinated, even in countries that recommend vaccination. Several studies have shown a higher risk of fatal hepatitis A and B infection when exposed to these viruses during travel and in patients with chronic liver disease and discussed the rationale of vaccinating these patients [5,37]. As some evidence of liver abnormality can be found in up to 92% of CF patients, they should all be considered a target group for vaccination. [38]. Hepatitis A infection is one of the most common vaccine-preventable travel infections and vaccination should be recommended to all those travelling to Southern Europe, Africa (including North Africa), South America, Asia and other overseas destinations. Transmission can occur through direct person-to-person contact, contaminated water, ice, shellfish, fruits, vegetables and other foods contaminated during handling, even at "standard" tourist accommodations. Although the risk of hepatitis B infection for international travellers is generally low (except for certain countries with a high prevalence), hepatitis B infection can, in contrast to the rather benign character of hepatitis A infection, result in a chronic carrier state and disease. Modes of transmission include contaminated injection or other equipment used for health care, dental and cosmetic procedures (tattooing and piercing), and, less known, unprotected sex and open skin lesions. CF travellers are more likely to need medical procedures during travel.

Hepatitis A vaccine is recommended for subjects older than one year. The combined hepatitis A and B vaccine, also recommended in subjects older than one year, offers dual protection in a simple schedule (0, 1, and 6 months) [37,39,40].

Yellow fever: transmitted by mosquitoes, and endemic in certain areas of Africa and South America (consult WHO country map). In some countries, proof of vaccination is required for entry. Yellow fever vaccine is a live virus vaccine that can be administered to subjects aged one year and older (in some exceptional cases also to infants aged 6–12 months). One injection offers a ten-year period of protection [39].

Other additional vaccinations, such as typhoid vaccine, cholera vaccine, tick-borne encephalitis vaccine, Japanese encephalitis vaccine, meningococcal ACWY vaccine, and rabies may be recommended for international travel. Additional information about these vaccinations can be found on the WHO web site [39].

2.5.3. Malaria

One of the most serious life-threatening diseases affecting international travellers. No vaccination is available yet. Detailed information about malaria risk and advice for chemoprophylaxis, as well as precautions for avoiding mosquito bites (application of DEET), is presented on the WHO web site. Medications used for prophylaxis in normal subjects such as mefloquine (Lariam®) and atovaquone/proguanil (Malarone®) can cause some digestive intolerance but do not seem to be hepatotoxic [39].

- When travelling, additional immunisations may be needed, depending on the destination. The required immunisations should be discussed with the CF doctor.

2.6. Destination: where to go and not to go

Choosing a travel destination depends heavily on the interests and readiness to assume risk of the patient and his/her relatives. Therefore, this document does not provide a list of recommended countries. In deciding on a destination, however, travellers should consider their current status as well as potential complications of their CF. Therefore, regions and countries with a good infrastructure and a high standard of health care should be given priority. Patients need to make themselves familiar with the facilities available in the country to which they are travelling. It is recommended that they consult the travel agency, the local health care arrangements and their CF centre prior to the journey. Patients should be informed about personal safety, required vaccinations, health insurance, local medical supply, AC adapter etc.

Ideally, comprehensive CF care via CF centres should be available in the destination country. This is the case particularly in the countries of the EU as well as Turkey, Israel, North America, the Far East, Australia and New Zealand. Travelling to non-EU countries in Eastern Europe, Russia, Mediterranean Maghreb countries, the Caribbean, South America (moderate or subtropical climate), or Islands in the Indian or Pacific Oceans is possible but requires detailed planning and information about regional/seasonal particularities and precautions. Strategies for dealing with potential complications (such as compiling lists of possible contact points, suitable transport services, etc.) should be developed prior to departure.

There is no official list available of specific countries/regions that CF patients should avoid visiting. In most cases, a good preparation of the journey is more important than the actual travel destination. However, patients should be aware of the risks involved in travelling to regions with uncertain medical service and hygienic standards; this includes, for example, regions with humid, tropical climate in South and Middle America, Africa and South-East Asia.

2.6.1. Lung infection

In the recent past, there have been several case reports on the specific risk for CF patients travelling to remote areas in tropical

Southeast Asia and Northern Australia. The basis of these warnings is the high frequency of *Burkholderia pseudomallei*, which occurs predominantly in fresh water and damp earth in Thailand, Malaysia, Vietnam and Northern Australia. This pathogen is known to cause symptomatic infections even in healthy people. There have been reports on severe pneumonias of CF patients who travelled to these regions [41–43].

- Certain areas bear a significant risk of specific infections, including *Burkholderia* pneumonia.

2.7. Infrastructure abroad (patient organisations, CF competence, hospitals)

Reliable information with respect to CF expertise and infrastructure (specialized care) at the intended destination is not always easy to find, often requires intensive research on the internet and may include contacting national patient associations or even specific clinicians within the worldwide CF community.

The Cystic Fibrosis Worldwide (CFW) web site provides a rather comprehensive list of most patient organisations across the world, including addresses and contact partners, with a focus on Europe, Russia, North Africa, South Africa, New Zealand, Australia, the United States and South America. Some parts of the world where no CF infrastructure is yet available are not included; however, contact partners are given for many of the countries that currently do not have a stable patient association (http://www.cfww.org/members/).

CFW also provides a list of CF clinics in e.g. Argentina, Australia, Belgium, Canada, the Czech Republic, Cuba, Denmark, Finland, France, Italy, Jordan, the Netherlands, New Zealand, Norway, Romania, the Slovak Republic, South Africa, Spain, Sweden, Switzerland and the United Kingdom. However, some of the clinics included in this list may not comply with the European Standard of CF care (http://www.cfww.org/members/).

The European Cystic Fibrosis Society (ECFS) provides a list of national CF associations and their web sites in Europe, Canada, Australia, New Zealand, Russia and the United States. Most of these web sites are in the respective national languages (http://www.ecfs.eu). Moreover, CF centres in the United States can be identified through the U.S. Cystic Fibrosis Foundation's web site (http://www.cff.org).

There are many other sites providing information on CF experts, clinics and CF associations. However, as with all web sites in general, their data may not be up to date, and contact partners change quickly. Therefore any addresses obtained from the internet should be verified before travelling and possible contacts discussed with the CF team.

2.8. CF health/travel insurance (incl. repatriation)

Treatment in foreign countries can be extremely expensive, and it is important to be well-informed about possible costs and their reimbursement when planning a trip abroad. There is no general regulation applying to everyone in all countries. Costs and reimbursement depend on the agreements between a patient's home country and the respective destination country, the regulations in both places, the type of treatment the patient needs and his/her health insurance plan. Gathering information prior to departure and scheduling enough time to acquire it is therefore essential.

2.8.1. European Union, Iceland, Liechtenstein, Norway and Switzerland

For EU citizens, treatment costs in any EU member country, as well as in Iceland, Liechtenstein, Norway and Switzerland, are covered by their national health insurance. However, this usually only includes those costs covered (reimbursed or partially reimbursed) in the patients' home countries. Consequently patients have to consider that expenses might be reimbursed only partially.

In order to receive care in the above countries, patients have to obtain the European Health Insurance Card, which is issued by the national health insurance companies. Depending on the respective national regulations and the treatment patients receive, they may have to pay for the treatment at the destination (before or after receiving it) and will be reimbursed later by their national health insurance, or the health care is provided for free. If patients are in doubt about the extent of the card's coverage for them, they are advised to contact their country's health authorities prior to departure for detailed information about what is covered and what will be reimbursed. A supplementary private insurance may be worth considering.

The European Union's DG Employment, Social Affairs and Equal Opportunities web site offers valuable information on the European Health Insurance Card and medical treatment abroad, as well as on various national contacts (http://ec.europa.eu/social/main.jsp?catId=509&langId=en).

Another useful source of information is the United Kingdom's National Health Service web site. It offers a country-by-country guide on how to access health care or claim refunds during a visit to countries in the European Union as well as Iceland, Norway and Liechtenstein. Although it addresses persons insured by the UK's NHS, this site provides valuable information for anyone preparing a trip abroad (http://www.nhs.uk/NHSEngland/Healthcareabroad/Pages/EEAcountries.aspx).

EU citizens can get free personalized advice from the European Union's Citizens Signpost Service which provides guidance and practical advice to citizens on specific problems they encounter in the EU and its Internal Market. Experts will clarify relevant rules, advise citizens on how to assert their rights and obtain, redress and direct them towards the body which can best help solve their problem (http://ec.europa.eu/citizensrights/front_end/index_en.htm).

2.8.2. Travelling to non-EU countries

If travelling outside the European Union, patients need to inquire with their national health authorities if there are any bilateral agreements concerning health insurance. If there is no such agreement or the coverage is not sufficient (which will usually be the case), patients will have to look for a private insurance plan.

In case patients are denied a private insurance plan because of CF, they should find out from their national health authorities if the national health insurance scheme provides any special regulations for chronically ill patients travelling abroad which still might cover treatment expenses in the destination country.

2.8.3. Repatriation

Insurance of the costs for repatriation has to be placed nationally. In some countries there may be non-profit organizations offering their members special services like repatriation without former personal health check.

- In Europe the European Health Insurance Card (EHIC) guarantees treatment to European citizens but some parts of the costs may not be covered by the national health insurance schemes. For travelling in non-European countries in most cases the patients will have to contract private health insurance plans. Finding suitable health insurance for the coverage of CF and other treatment costs and for repatriation can be tricky, and patients should think about it carefully prior to departure.

2.9. Specific documents (customs, forms, medical letter)

Several documents issued by the patient's CF clinic may be helpful during travel and in emergencies:

A certificate for customs stating why the person needs a large supply of drugs and medical devices abroad, among them syringes and needles. This document helps to cross borders and pass medication through airport security checks. The document should contain: patient's name and date of birth, general description (not name) of the disease ("chronic pulmonary disease"), a list of medication, approximate quantities needed and daily frequency, a list of medical devices, physician's name and signature, stamp of the physician/clinic to make the document official. A template of such a certificate can be downloaded at http://ecorn-cf.eu/index.php?id=265&L=8.

A detailed medical report in English facilitating treatment abroad.

The document should contain: patient's name and date of birth, address and contact details of the patient's CF clinic and attending physician, name of the underlying disease and a short description, the person's health status, known allergies, the daily (physio)therapy, a list of medications, approximate quantities needed and daily frequency, stamp of the physician/clinic to make the document official. A template of such a "medical report" can be downloaded at http://ecorn-cf.eu/index.php?id=265&L=8.

A certificate for theme and attraction parks. In some theme parks such as Euro Disney, people with a handicap or chronic condition like CF can obtain a special pass granting them priority access to attractions by enabling them (and usually one or more accompanying person) to skip waiting lines. An official document signed and stamped by a clinic and stating the condition or handicap (from national health authorities) or a paper mentioning the disease and the need to prevent long standing times and dehydration are usually accepted in order to obtain this pass. Patients should contact the park they intend to visit to find out what its criteria are.

Table 3
Recommendations for drug storage.

Substance	Storage recommendation	Comments/side effects
Antibiotics		
Colistemethate p.i.	Do not store above 25 °C	
Tobramycin p.i.	Store between 2° and 8 °C	Stable for 28 days at 25 °C or below
Azithromycin	No special storage conditions apply	
Chloramphenicol	Store in a cool, dry place	
Doxycycline	Store below 25 °C	May cause photosensitivity
Ciprofloxacin	No special storage precautions	May cause photosensitivity
Flucloxacillin	Store in a cool dry place	
Inhaled therapies		
Sodium chloride 0.45%	No information	Short dated
Dnase	Store between 2° and 8 °C	• Brief exposure (up to 24 h) to up to 30 °C does not affect stability, and drug may be returned to the fridge afterwards. • Protect from light
Salbutamol nebs	Store below 30 °C	Protect from light
Colistin		Protect from light
Tobramycine	Store between 2° and 8 °C	• Protect from light • Stable for 28 days at 25 °C or below
Hypertonic saline 4.5%	Store below 25 °C	May cause bronchoconstriction
Digestive medications		
Pancreatic enzymes	Do not store above 25 °C	
Miscellaneous		
Ursodeoxycholic acid	• Store Urdox film coated tabs below 25 °C • No special requirements for destolit or ursofalk brand	Urdox should be stored in original container
Tranexamic acid	Do not store above 25 °C	

Furthermore, patients should have the following information at hand when travelling:

insurance policy and data, address and contact partners of insurance agency (national and private), contact data of care-taking CF clinic, contact data of national patient association any medical documents if necessary, important telephone numbers in case of emergency.

- CF patients should always carry their CF specific insurance and health information as well as all necessary contact data.

3. During the journey and on site

3.1. Transportation and storage of medications

If carrying medical supplies, such as medications, needles and syringes, patients should always carry a letter from their doctor describing the underlying disease and listing all supplies and approximate quantities needed. See Section 2.9 for further information.

All medicines and devices need special consideration on flights. If devices which require needles are to be used on board, patients have to carry their own disposal unit. If possible, all medicines should be kept in hand luggage. If the quantities are too large, patients are advised to keep enough medicines and equipment in their carry-on baggage to last for up to one week in case suitcases are lost in transit. Baggage holds for check-in baggage may be below 0 °C, which may have consequences for temperature sensitive medicines and might cause glass vials to break. One option is to ask the airline if a larger bag may be carried on or if a bag may be stowed at the gate when boarding.

Other respiratory-related equipment and devices (e.g. nebuliser, CPAP, and BiPAP machines) might be carried but not operated during the flight. For specific information on oxygen supplementation devices see Section 2.4.

Specific storage of medicines at the travel destination depends on many different factors and patients are advised to check with their travel agencies or companies to ensure their needs can be met. They should also take into consideration before travelling that some of the medicines needed may not be available in the destination country. A list of some commonly used medications in CF along with information on stability and storage is shown in Table 3. Please note that not every single medication is covered in this overview. Patients are therefore advised to consult with their doctor about specific questions they may have.

- Some CF medication needs specific storage precautions. The CF individual should discuss these specific requirements with the CF centre pharmacist.

Table 4
Drug photosensitivity.

Drug (in alphabetical order)	Photosensitivity Yes/No
Amoxicilin/Clavulanate	No
Azitromycine and other macrolides (erytromycine, klaritromycine)	Yes (but rare)
Cefuroxim and other cephalosporins (cefaclor, cefalexin)	No
Ciprofloxacine	Yes
Chloramphenicol	No
Dnase (Pulmozyme)	No
Doxycycline	Yes
Fat solubile vitamins (ADEK)	No
Fluconazole	Yes
Itraconazole	Yes
NSAID (non steroid antiinflammatory drugs)	Yes
Pancreatic enzyme supplements (Kreon)	No
Sulfamethoxazol/Trimethoprim	Yes
Tetracycline	Yes
Voriconazole	Yes

Comment: The list is not complete. If there is uncertainty about photosensitivity of a drug the traveller should ask the CF doctor or pharmacist.

3.2. Routine therapy and medication

For many people with CF, taking a break from everyday life also means taking one from routine therapy. Each current therapy should be adapted to the travel situation in consultation with a CF specialist. If possible, equipment and medications should be rationalized to ensure the best possible quality of life while travelling, i.e. the treatment regimen should be reviewed to optimize the benefits of travel balanced with the medical need for each medication and treatment. Antibiotics can be taken along as stand-by medication. They can also be taken throughout the trip as a prophylaxis for exacerbation. Patients should be informed about possible side effects of the medications. (NB: Some antibiotics and antimycotics may cause a severe photosensitive rash, and patients are advised to use extra protection such as sun block, a hat, etc. Table 4 provides an overview of some drugs that may cause photosensitive reaction.)

The patient's diet at the destination may differ from the one he/she is used to at home. For patients suffering from pancreatic insufficiency, the adapted intake and dosage of pancreatic enzymes at the destination should therefore be discussed prior to departure. The same goes for patients with diabetes mellitus that requires therapy. Increased movement and potential alcohol consumption at the destination may lead to an alteration of the blood sugar homeostasis. In this case, it is important to prevent hyperglycaemia and hypoglycaemia, and the patients should always have carbohydrates readily available. Fellow travellers should always be informed about diabetes mellitus, signs of hypoglycaemia, and appropriate counteractions.

- CF medication may need adaptation according to climate change.

3.3. Airway clearance

How much and what type of airway clearance is appropriate while travelling should be discussed with the CF physiotherapist. There may be some difficulty adhering to airway clearance while travelling, especially if taking long-haul flights, keeping long hours and constantly being on the move. Action points should be given to improve adherence, e.g. asking travelling companions to give reminders or assist with airway clearance. Available evidence suggests that no airway clearance regimen has been shown to be better than any other. In patients who use bulky equipment for airway clearance, this evidence would support using an alternative and equally effective regime during travel. For example, a vest could be substituted with a more portable device such as PEP, acapella or flutter.

Most nebuliser systems can be used in any country as long as there is suitable power supply. Some can even be plugged into a cigarette lighter or are battery-operated. A range of systems are available that make travel abroad easier as they are portable and lightweight; however, some do need an adapter. In general in Europe (except for Cyprus, Gibraltar, and Malta), the voltage for the nebuliser is not a problem (220 V) and a standard travel plug adapter is all that is needed. If travelling to the USA, South America, the Caribbean, Cyprus, Gibraltar, and Malta, a 110 V nebuliser is needed. On long-haul flights, battery operated compressors can be used on board, but it is important to check with the airlines about this. Some airlines carry their own compressors, but their use is not recommended for hygienic concerns. In general, compressors should be carried as hand luggage. Like other medications, nebulised drugs should be carried as hand luggage as well in case of need during the journey or in case of delay. A letter from the patient's CF clinic stating the purpose of a nebuliser and compressor, and a list of all medications is recommended for customs [44–46]. See Section 2.9 for further information.

- Nebuliser and other equipment should be checked for electrical compatibility.

3.4. Prevention of salt depletion and dehydration

Physical activity has been recognised as beneficial to patients with CF. When exercising in the heat, patients have to take into account potential risks. A low tolerance of CF patients to climatic heat stress has been described [47–49]. Because they have up to three times higher concentrations of sodium and chloride in their sweat, serum osmolality becomes lower compared to healthy controls when exercising in hot conditions and drinking pure water [50]. This relative hypoosmolality deprives the patients of a trigger from thirst, leading to an underestimation of their fluid needs and "voluntary dehydration" [51].

Prevention of dehydration should be achieved through high salt intake [52] and regular fluid replenishment rather than relying on patient's thirst. One hour before exercising, CF patients should drink 400–600 ml of fluids [53]. During prolonged activities, 200–300 ml should be consumed every 15–20 min [53]. If activities last 45 min or less, fluid intake can be postponed until after the training. Under warm or hot conditions, there is an increased risk of salt loss and dehydration, requiring additional fluid intake [54]. Oral rehydrants containing from 4% up to 12% carbohydrates, a sodium chloride concentration of 50 mmol/l (equal to 2.9 g of salt per litre), as well as potassium and bicarbonate are useful and should be prescribed to all CF patients for travel abroad. It has to be taken into account that most commercial drinks contain only 18 mmol/l sodium chloride (equal to about 1 g salt per litre). However, it has been shown that only drinks with a salt content of 50 mmol/l enhanced drinking and attenuated voluntary dehydration [52]. Therefore, individuals with CF are advised to add a pinch of salt to their beverages [53] or to consume commercially available energy drinks containing salt supplements. Salt replacement following exercise might also be augmented by slow release tablets such as Slow Sodium (600 mg), which contain 10 mmol of sodium chloride in an enteric-coated tablet. The prescription for adults is usually 1200 mg twice a day when going to a hot destination. This dosage can be increased to four times a day (max. dose 20 tablets/day), depending on the temperature and the amount the individual patient perspires [55]. However, the tablets may cause gastric discomfort and are not suitable for use during exercise. In addition to the above, patients should eat salty snacks and keep themselves mobile, especially on long-haul flights. Due to the low humidity on board, there is an increased risk of dehydration during air travel. This, together with decreased mobility during the flight, constitutes an increased risk of deep venous thrombosis, with the danger of pulmonary artery embolism. Relative contraindications to high volume load in patients with liver cirrhosis with ascites must be respected.

Diabetics in particular are in danger of fluid loss and dehydration in hot regions. Additional fluid loss in cases of diarrhoea and vomiting should be balanced by taking electrolyte solutions in order to prevent DIOS.

- For people with CF a sufficient supply with fluids and salt should be provided when travelling and especially exercising in hot conditions. It is not sufficient to rely on the patient's feeling of thirst and the salt content of commercial drinks is usually not adequate.

3.5. Physical activities and sports

Just like healthy people, many CF patients use their holidays and leisure time for outdoor physical activities and sports. It is indisputable that such activities have a favourable influence on many aspects of CF. Active travel involving sports such as skiing, snowboarding, water sports, scuba diving, or bungee jumping are becoming increasingly popular. As there are no systematic investigations on the different kinds of CF-specific

risks associated with the different types of sports, no evidence-based recommendations can be made at this point in time. The following recommendations are mainly based on case reports and are therefore anecdotal; however, patients should be made aware of these hazards before attempting some of these activities (see Table 5, a shorter version of "Potential complications of sports activities" at http://ecorn-cf.eu/index.php?id=265&L=8).

Exercise-induced hypoxemia: Altitude can lead to a decrease of oxygen saturation in the blood, therefore winter sports and climbing at high altitudes are not recommended for patients with a decrease in oxygen saturation below 90% during exercise test [55]. Episodes of acute right heart failure at high altitude are well documented [55,56]. It is advisable to do an ergometry with every patient before starting a sports program and to include one in the annual check-up program. No monitoring is needed in patients with a normal result of the incremental maximal exercise test [53]. Exercise that leads to a decrease in oxygen saturation of more than 5% or below 90% should be avoided [57,58]. Patients with an oxygen saturation below 90% at rest are at risk of worsening and should not engage in physical activities without supplemental oxygen and close supervision of oxygen saturation during exercise.

Table 5
Potential complications of sports activities. Please note that this table is only supposed to provide a basic overview of the risks involved in some of the most popular types of sports. A more detailed table including specific recommendations is available for download at http://ecorn-cf.eu/index.php?id=265&L=8. In general, exercise is beneficial, but patients are strongly advised to consult with their doctor about potential complications resulting from their sport of choice in their specific health condition.

Sports	Complications
Ball sports	*Bleeding* from oesophageal varices
Soccer, volleyball, tennis, etc.	*Rupture* of liver and spleen
	Fractures (esp. in team sports)
	Pneumothorax (Tennis)
Contact sports	*Bleeding* from oesophageal varices
Judo, karate, etc.	*Rupture* of liver and spleen
	Fractures (esp. in team sports)
Water sports	*Pseudomonas* (in pools, etc.)
Swimming, scuba diving, etc.	*Pneumothorax* (diving)
Extreme sports	*Pneumothorax*
Bungee jumping, parachuting, free climbing, etc.	*Bleeding* from oesophageal varices
	Rupture of liver and spleen
	Fractures
	Exercise-induced hypoxemia (climbing at high altitude)
	Acute right heart failure (climbing at high altitude)
Winter sports	*Exercise-induced hypoxemia*
	Acute right heart failure
	Pulmonary exacerbation
Horse riding	*ABPA*
	Pseudomonas
Strength training with high loads	*Pneumothorax*
	Haemoptysis
Sprinting	*Haemoptysis*
Endurance training	*Hypoglycaemia* in diabetes
	Dehydration and hyponatriaemia
Sauna/Hot tubs	Pseudomonas

Bronchoconstriction: There is some data showing a bronchial hyperreactivity in CF patients, which is mostly induced by provocation with chemical agents. Whether or not exercise itself induces bronchoconstriction in CF patients is less clear. For some patients with a history of exercise-induced bronchoconstriction, positive effects can be achieved through the use of beta-2-agonists before exercise. The effect of such a therapy should be evaluated prior to travelling [53].

Pneumothorax: Patients with advanced lung disease should not engage in sports that require press breathing or rapid and jerky movements of the upper body (e.g., tennis, volleyball, and bungee jumping). Deep-sea and scuba diving is contraindicated in patients with air trapping, which may lead to pneumothorax on ascent or aggravation of sinus disease [55,59]. As air trapping can be seen even in clinically healthy CF patients and a pneumothorax under water is a potentially life-threatening situation, it seems reasonable to disadvise CF individuals to actively engage in scuba diving.

Haemoptysis: Patients with bronchiectasis and a history of haemoptysis should avoid those types of sports with a strong increase in breathing or blood pressure (e.g., sprinting, strength training with heavy loads); oxygen supplementation during training might reduce the risk in patients with exercise-induced hypoxaemia, as it can reduce the breathing volume per minute for a given strain [53].

Right heart failure: In patients with increased right heart strain, physical activity and sports could lead to acute cor pulmonale, heart insufficiency or ventricular arrhythmias [59,60]. Physical activities at high altitude are not recommended for CF patients who are already hypoxic, as aerobic and anaerobic exercises at altitude cause episodes of right heart failure. Two cases of cor pulmonale requiring heart and double lung transplantation after strenuous exercise during holidays at altitude have been reported in the literature [56]. In the presence of chronic cor pulmonale, physical activities should be performed cautiously and under strict supervision [59].

Hypoglycaemia: Physical activities and endurance training can result in significant decrease in blood glucose, particularly in patients who are on insulin or oral anti-diabetics therapies. There are also sporadic reports of hypoglycaemia following exercise in non-diabetic patients. It is recommended that patients have a meal rich in carbohydrates before exercise and adjust their insulin doses [53]. During prolonged moderate to heavy exertion, patients with diabetes should frequently measure their blood glucose level.

Bleeding: As life expectancy is increasing, the prevalence of adult patients with advanced liver disease (cirrhosis, impaired plasmatic coagulation) increases. Sports with acute changes of pressure in the abdomen or thorax (e.g., contact sports with risk of blows in the abdomen like soccer, judo, and karate) or changes of blood pressure (e.g., strength training with heavy weights, etc.) are associated with the risk of rupture of liver and/or spleen, as well as gastrointestinal bleeding from oesophageal varices [55].

Fractures: Many older CF patients show a significant reduction of bone density. Patients who are playing sports where the risk of fracture may be considerably increased should

pay particular attention to this fact. For them, sports with a risk of over- and downthrow (e.g., contact sports and some martial arts, bungee jumping, and parachuting) are not recommended [61–63].

- Some sports have specific risks—some health conditions preclude specific sports. The risk associated to specific sports activities should be discussed between the individual with CF and the CF centre.

3.6. Prevention of *P. aeruginosa* infection

Although acquiring *P. aeruginosa* is not an issue specific to travel it is nevertheless a major concern for many patients when taking a trip. As in daily life, the possibility of acquiring *P. aeruginosa* or other CF-relevant bacteria during travelling cannot be completely avoided. The general concern of lower hygienic standards abroad (e.g. bacterial load of sanitary facilities, swimming pools) seems to be of importance. However, the basic hygienic recommendations and precautions CF patients should follow abroad are somewhat similar to those at home. It has to be kept in mind that evidence for most recommendations below is modest at best.

3.6.1. From the environment

Most water reservoirs are natural habitats of *P. aeruginosa*, including sea shores, lakes and rivers. However, there is ongoing controversy about to what extent these sources pose a risk of CF-related lung infection. Whether or not the use of swimming pools should be discouraged is also under debate. Most CF centres allow their patients the use of public pools that are certified by local health authorities. However, the risk of bacterial transmission might be related to the practice used for water disinfection, which differs throughout Europe: The prevalence of *P. aeruginosa* in public swimming pools was reported to be 4–7% in Switzerland [64]. In contrast, a study from Northern Ireland detected *P. aeruginosa* in up to 38% of public swimming pools [65]. In the latter study, the prevalence of *P. aeruginosa* was even higher in private pools and jacuzzis (whirlpools) (72%). There was a similar trend in respect to public and private hydrotherapy pools. Therefore, CF patients should weigh the risk before using private pools or spas.

P. aeruginosa can often be isolated from the peel of fresh fruit, vegetables, and salads. Therefore, it is recommended that patients with CF wash, peel or cook vegetables before consumption.

Many animals are known carriers of *P. aeruginosa* too, such as nematodes, minks, dolphins, and horses. The latter frequently carry *P. aeruginosa* in their noses, and there is a risk of transmission during horse riding [66]. Also, acquisition of Aspergillus spp. from stable manure has been reported.

3.6.2. Patient-to-patient transmission

In contrast to the environmental sources described above, transmission of bacteria between CF patients is well characterized. In the past, it was found beneficial for CF patients to engage in social activities, such as summer camps, together. Positive effects of such camps on patient exercise tolerance, nutritional status, and well-being were reported [67]. This attitude has changed since evidence of cross-infection of bacteria, particularly *P. aeruginosa* and *B. cepacia* has come to light. Nowadays, the risk of cross-infection is thought to outweigh the possible benefits and CF summer camps have been discontinued [4,68–70].

However, when attending events with other CF patients, it is important to minimise the possibility of cross-infection by following certain hygienic guidelines (please see http://cfww.org/docs/conferences/2009/hygiene_guidelines.pdf). [71]. There is broad consensus that individuals who have cultured positive with *Burkholderia cepacia* complex, Methicillin resistant *Staph. aureus* (MRSA) or other panresistant bacteria should not be in close contact with other CF patients or attend CF events [72].CF patients should discuss cross-infection issues with their physician and make an informed decision about whether to engage in social activities with other CF-patients or not.

4. Specific recommendations for immunocompromised travellers/organ recipients

Immunocompromised CF patients after lung or liver transplantation need special advice before travelling. While no specific literature regarding travellers who received a lung or liver transplant is available, there are reports that focus on risks and recommendations for immunocompromised travellers, including solid organ recipients. Three basic problems have to be distinguished here: first, increased susceptibility to travel-related diseases and opportunistic infections; second, drug interactions between routine medication (e.g., immunosuppressants) and concomitant medication for travel-related illnesses (e.g., malaria prophylaxis); and third, concerns regarding vaccine use (e.g., safety of live vaccines, potentially decreased vaccine efficacy).

4.1. Diseases related to travel

Most commonly, travel-related diseases are foodborne infections associated with food handling practices. Some specific bacterial infections, such as non-typhoidal *Salmonella* spp., *Shigella* spp., *Campylobacter* spp. and *Microsporidia*, are more severe in immune suppressed hosts [73–75]. While recognizing the limitations of "food and water precautions," immunocompromised travellers should be advised to follow them rigorously, e.g. by having hot meals in restaurants, taking water precautions (bottled, boiled, and filtered), and avoiding unpasteurized milk products. Every immune suppressed traveller, particularly those with pre-existing renal dysfunction or on nephrotoxic medication (e.g., Cyclosporin A), should be aware of the importance to maintain hydration and options of oral rehydration. Prophylactic antimicrobial agents are not routinely recommended but might be used for a limited period of time. Patients should carry a stand-by supply of antibiotics (e.g., Ciprofloxacin, Azithromycin, and Metronidazol) and be advised to start medication early in the case of fever or diarrhoea. The threshold for seeking qualified medical advice

and discontinuation of vacations in case of deterioration of health should be set low.

- Immunocompromised CF patients should be carefully advised to avoid risk of opportunistic infections.

4.2. Drug interactions

Many routine drugs prescribed to transplant recipients interact with drugs that are metabolized by CYP3A4 system. For example, malaria prophylaxis with chloroquine increases serum levels of Cyclosporin A, FK 506 (tacrolimus), or Rapamycin. However, the data on interactions between anti-rejection drugs and most travel-associated drugs are limited. It is recommended that patients start concomitant medications (e.g., malaria prophylaxis) several weeks prior to travelling in order to monitor and adapt the serum levels of immunosuppressants.

4.3. Vaccination under immunosuppression

Any recent or present immunosuppressive treatment including oral corticosteroids longer than one month with high doses may compromise the efficacy of any vaccine and may be a danger in live vaccines of contracting the disease. Inhaled steroids, except in very high doses, are not a contraindication to vaccine administration [5].

Following lung or liver transplantation, any proposed vaccine should be considered from two perspectives: safety as well as the possibility of decreased effectiveness in the context of the underlying immunosuppression. In general, live vaccines should strictly be avoided in the immunosuppressed CF patient. Varicella vaccine, oral poliomyelitis vaccine, measles–mumps–rubella vaccine, yellow fever vaccine and BCG are the most common live vaccines. However, the risk of the exposures of the disease must be balanced against the risks of vaccination, and the individual's degree of immunosuppression. Therefore it is very important for any future transplant candidates to have a vaccination review before transplantation [5,76]. Scheduled vaccinations should be completed at least two weeks before transplantation.

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