CLINICAL REVIEW

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Advising on travel during pregnancy

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As travel increases, ¹ the number of pregnant women who travel will probably rise. Women often ask if travel is safe in pregnancy and seek advice from a range of healthcare professionals. Travel related maternal and fetal morbidity and mortality can be completely avoided only by postponing travel until after delivery, but travel may be necessary or desirable during pregnancy.

Most women are "low risk" and can expect no problems with travel during pregnancy. However, there are particular risks to be considered with each stage of pregnancy, especially if the pregnancy is complicated by comorbidity. Medical concerns can be divided into risks of travel itself (in particular air travel), difficulties related to negotiating different healthcare systems and insurance, and specific risks of acquiring infectious diseases in particular countries. Some travel companies place restrictions on travel in pregnancy. Limited robust evidence or disseminated guidelines makes it difficult to provide definitive advice.

When asked to advise a woman regarding travel in pregnancy a careful risk assessment will help to inform the advice given. We outline an approach to considering risks associated with travel during pregnancy and discuss preparation for travel, advice on managing illness while abroad, and relevant post-travel considerations. This article is relevant to all who provide care during pregnancy, particularly general practitioners, who may be the primary source of advice for women with uncomplicated pregnancies who are considering travel.

What are usual restrictions on travel in pregnancy?

Many domestic and international airlines place restrictions on travel at advanced gestations (box 1), although guidelines vary between airlines. Women should consult their airline before flying to check individual restrictions. Some ferry operators have similar regulations to airlines, but most international train services are not restrictive.

Box 1 | Typical gestation guidelines for air travel in uncomplicated pregnancies

- Unlimited up to 28 weeks
- After 28 weeks women should carry a letter from a doctor or midwife confirming the due date and that pregnancy is uncomplicated
- Singleton pregnancies: flying usually permitted up to 36^{+6} weeks*
- Multiple pregnancies: flying usually permitted up to 32*6 weeks*
- *Women must inform and check with the individual airline on every occasion.

Who is at increased risk of adverse outcome and when?

No formal evidence or guidance is available on absolute contraindications to travel in pregnancy, because the decision may depend on gestation, degree of clinical compromise, and presence of pre-existing comorbid disease. However, certain women with obstetric or medical conditions should be advised against travelling (table 1); this decision will need to be made on an individual basis by an obstetrician, often in conjunction with the relevant medical specialist, and will depend on the degree of potential compromise.

In women who are otherwise healthy, and when travel dates are flexible, doctors are often asked if there is a "best" gestation for travel. Each trimester has specific risks and considerations.

First trimester

Although travel probably does not alter risk in women who are at increased risk of having an ectopic pregnancy or a miscarriage it will increase the difficulty (and cost) of management if either of them occurs. Women at increased risk of an ectopic pregnancy include those who have become pregnant after sterilisation or while using an intrauterine contraceptive device and those with previous ectopic preg-

SUMMARY POINTS

Travel during pregnancy may carry additional risks

The second trimester of pregnancy is considered the safest in which to travel

Air travel may carry risk of miscarriage, preterm birth, and thromboembolism

Adequacy of obstetric and neonatal care facilities at destinations is varied

Women should obtain adequate insurance and check with their airline for restrictions on travel

Communicable diseases acquired abroad may increase risks of perinatal morbidity

SOURCES AND SELECTION CRITERIA

We searched PubMed and the Cochrane Library using the terms "travel", "travelling", "flight", and "flying" together with "pregnancy" and "antenatal", along with other relevant search terms for specific topics. We also searched the National Institute for Health and Clinical Excellence (NICE), the Royal College of Obstetricians and Gynaecologists (RCOG), and the American Congress of Obstetricians and Gynecologists (ACOG) for published guidelines and articles yielded by reference lists.

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Table 1 Indications for caution before travel		
Conditions	Risk	
Obstetric		
Pregnancy of unknown location	Ectopic pregnancy	
Recent invasive procedure (such as amniocentesis)	Miscarriage	
Severe anaemia or haemoglobinopathy	Fetal hypoxia at reduced partial pressure of oxygen	
Multiple gestation	Preterm delivery	
Gestational hypertension	Progression to pre-eclampsia	
Fetal growth restriction	Fetal compromise	
Placenta praevia	Serious haemorrhage	
Previous preterm delivery	Recurrent preterm delivery	
Medical (if poorly controlled)		
Maternal heart disease	Decompensation	
Chronic hypertension	Severe hypertension, progression to pre-eclampsia, fetal growth restriction, placental abruption	
Diabetes	Hypoglycaemia or hyperglycaemia, need for adjustment of timings of insulin if crossing time zones	
Epilepsy	Seizures	
High risk of thrombosis	Thromboembolic event	

nancy, tubal surgery, pelvic inflammatory disease, infertility, and documented tubal pathology.

A review noted that the miscarriage rate is 3-30% for women who experience vaginal bleeding in the first trimester. Prospective studies quote a miscarriage rate of only 3-5% if fetal heart activity is confirmed after bleeding. ³

Second trimester

Pregnancy related complications, including miscarriage, are less common during the second trimester of pregnancy than in the first and the third trimester. Risks of an adverse pregnancy outcome are small and similar in nature to those described for the third trimester. The National Institute of Health and Clinical Excellence (NICE) schedule for antenatal care advises only one visit in the second trimester, after the 20-22 week anomaly ultrasound scan.⁵

Third trimester

Preterm delivery (spontaneous and iatrogenic, as a result of pregnancy complications) occurs in 7-12.3% of all pregnancies, ⁶ ⁷ depending on country of residence and ethnicity, but is often unpredictable. Women at increased risk of preterm delivery include those who have had a preterm birth, recurrent episodes of threatened preterm delivery, multiple pregnancy, or cervical trauma.

What are the specific risks associated with air travel?

Specific concerns have been raised about the safety of air travel during pregnancy as a result of the woman's changing physiology and the altered environmental conditions.

Miscarriage and preterm birth

A recent meta-analysis of nine studies, mainly retrospective cohort in design, reported that the risk of pregnancy loss was significantly greater in flight attendants than in controls (odds ratio 1.62, 95% confidence interval 1.29 to 2.04). Risk of preterm birth (less than 37 weeks) was also significantly higher in air passengers than in controls (1.44, 1.07 to 1.93), but not in flight attendants (1.37, 0.85 to 2.22). The authors note that studies were few in number and generally not of high methodological quality.

Venous thromboembolism (box 2)

Venous thromboembolism is 10 times more common in pregnant women than in matched non-pregnant women, and it complicates about one in a 1000 pregnancies. Inherent prothrombotic endothelial changes of pregnancy and relative obstruction to venous flow by the gravid uterus contribute to this. Travel may confer further risk of thrombosis because of immobility, low oxygen tension, and low humidity, which lead to venous stasis and dehydration. ¹⁰

A recent cohort study reported that air travel was associated with a two to four times higher risk of a new thrombosis in non-pregnant people. 11

Exposure to radiation

Exposure to radiation at any stage in pregnancy, but particularly during fetal organogenesis, is of concern. Exposure to cosmic radiation during flight is potentially greater than on the ground. Guidelines for diagnostic imaging in pregnancy from the American Congress of Obstetricians and Gynecologists (ACOG) conclude that there is no known increase in fetal malformations or miscarriage or effects on growth at levels less than 50 mSv. 12 For comparison, the estimated cumulative background radiation per year in the United Kingdom is 2.2 mSv, a chest radiograph gives 0.1 mSv, and the radiation exposure from a 10 hour flight is estimated to be 0.05 mSv. 13 The risk of adverse effects to the fetus from radiation during a single flight is negligible, but pregnant women who are frequent fliers, and airline staff who fly, may reach levels of exposure over the recommended maximum.

Low oxygen saturation

The partial pressure of oxygen in inspired air in aeroplane cabin environments maintained by cabin pressure is usually lower than it is at sea level. Physiological adaptations to this relative reduction in inspired oxygen include an increase in heart rate, increased blood pressure, and a decrease in transcutaneously measured arterial oxygen saturation. ¹⁴ Fetal haemoglobin has a greater affinity for oxygen than does adult haemoglobin, and the fetus is able to maintain a higher oxygen saturation in this environment, which protects it during routine flight conditions. Most healthy pregnant women will have no adverse effects, but those with pre-existing cardiovascular problems, sickle cell disease, or severe anaemia (haemoglobin <80 g/L) may

Box 2 | Royal College of Obstetricians and Gynaecologists' recommendations for flight deep vein thrombosis prophylaxis¹⁰

Use aisle seat if possible to facilitate movement Mobilise throughout flight—every 30 minutes Avoid dehydration

Increase water intake

Limit caffeine and alcohol intake

Consider elastic compression stockings for flights longer than four hours

Consider low molecular weight heparin in the presence of additional risk factors for deep vein thrombosis (such as obesity, previous deep vein thrombosis) if not already on antenatal thromboprophylaxis

experience the effects of low arterial oxygen saturation. ¹⁵ A routine haemoglobin check before travel is not currently recommended, but women with known anaemia should aim to optimise their haemoglobin before they travel, and those with severe anaemia should be advised to postpone air travel.

What are the risks from communicable diseases?

Travel to many developing countries puts pregnant women at increased risk of exposure to communicable diseases that manifest more severely in pregnancy. Prophylaxis and treatment of infectious diseases may affect the fetus. Although the risks of communicable diseases should not be exaggerated, because most are rarely acquired, important examples include the following.

Travellers' diarrhoea (box 3)

Travellers' diarrhoea affects 10-60% of visitors to tropical and semi-tropical regions of the developing world. ¹⁶ In pregnancy, decreased gastric activity and slowed intestinal

Box 3 | Travellers' diarrhoea18

Prevention

Meticulous care with hand washing and attention to food hygiene are needed

Use boiled or bottled water (theoretical risk with iodine water purification and fetal toxicity)

Avoid raw food (such as vegetables) not washed in a known safe water source

Treatment

Most patients will respond to early and generous oral rehydration (oral rehydration salts mixed with filtered water, which is safe in pregnancy). Use a sugary drink if oral rehydration salts are not available because sugars are likely to increase water absorption

If the patient does not respond, consider treatment for atypical pathogens (such as giardia, amoeba, and cryptosporidia) after confirmed diagnosis on a stool sample; check safety of specific antibiotics in pregnancy Early recourse to parenteral rehydration if the patient does not respond to oral fluids

Box 4 | Assessment of a pregnant woman before travel

Assess the index pregnancy

Has the woman considered gestation specific risks? Are blood pressure, antenatal progress to date, and ultrasound findings normal?

Does the woman have acute symptoms or signs (vaginal bleeding, uterine activity, pain)?

Are the risks of antepartum haemorrhage, preterm labour, and pre-eclampsia low?

Check history of problems in a previous pregnancy Have the risks of recurrence been considered?

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$Check\,pre-existing\,or\,additional\,medical\,conditions$

Is acute deterioration likely during travel?

Is the woman carrying appropriate documentation?
Drugs: does the woman have sufficient supplies
(including needles), has she considered the effects of
crossing time zones (for example, with insulin), and can
she replace supplies if necessary?

transit may result in more severe dehydration and ketosis, which may increase the risk of premature labour. ¹⁷

Malaria in pregnancy

Malaria in pregnancy carries substantial risks to mother and baby, particularly with *Plasmodium falciparum* infection. Pregnant women probably have a higher risk of being bitten by mosquitoes than non-pregnant women¹⁹; an increased risk of contracting malaria and dying from it²⁰; a higher likelihood of malaria related hypoglycaemia²¹; and an increased risk of miscarriage, stillbirth, and premature labour if they develop malaria.²² Malaria prophylaxis is not 100% effective.¹⁰

Other infections

Hepatitis E is a faeco-oral hepatitis virus that is more likely to cause severe disease in pregnancy. There is currently no vaccine. The incidence of rubella is higher in many countries than in the United Kingdom; women who have not been vaccinated or infected in childhood are at increased risk of acquiring rubella. Acquiring HIV during pregnancy produces a high viral load, making mother to child transmission of HIV more likely. Many rarer infectious diseases ranging from typhoid to listeriosis pose a greater risk to the fetus, the mother, or both when acquired during pregnancy.

What pre-travel advice should you give after assessing risk?

Box 4 summarises the approach to risk assessment in pregnant women who are considering imminent travel.

Women considering air travel

The Royal College of Obstetricians and Gynaecologists (RCOG) and the ACOG have both issued guidance on air travel in pregnancy. The ACOG states that healthy pregnant women with uncomplicated singleton pregnancies can fly safely up to 36 weeks' gestation.¹⁵ Similarly, the RCOG guidelines state that there is no specific risk to pregnancy associated with commercial air travel. 10 However, NICE suggests that pregnant women should be informed of the risk of venous thrombosis with long haul air travel, although it is unclear whether pregnancy confers an additional risk.⁵ The RCOG recommends prophylactic measures for pregnant women against venous thrombosis (box 2), including the use of correctly fitted compression stockings, which reduce the risk of thromboembolism in the general population, 10 although no evidence exists on their effectiveness in pregnancy. Women with pre-existing cardiovascular problems, sickle cell disease, or severe anaemia should either not travel by air or they should consider supplemental oxygen if travel is unavoidable.

Women should be advised to wear a seatbelt while seated (whether travelling by aeroplane, car, or coach), strapped low under the abdomen, across the top of the thighs.¹⁰

Women consulting early in pregnancy

The location of the pregnancy should be confirmed ultrasonographically before travel in women who are at increased risk of miscarriage or ectopic pregnancy. In the

UNANSWERED QUESTIONS

- Is there a true increased risk of miscarriage among frequent flyers?
- What is the increased risk of thromboembolic disease in women who fly during pregnancy and how can it be reduced?
- Can the risk of preterm labour be predicted accurately before travel using a combination of cervical length and cervicovaginal fetal fibronectin?
- Can the risk of pre-eclampsia be predicted accurately before travel using a combination of biomarkers (plasma or urine) or uterine artery Doppler velocimetry, or both?
- Should the NHS bear the cost of additional investigations to support the mother's decision to travel while pregnant?

A PATIENT'S PERSPECTIVE

During my first pregnancy I travelled to Sri Lanka to be with my husband's family who were organising a family reunion. I was 23 weeks' pregnant and my five month scan had been fine. While I was out there I was careful about what I ate and drank but I still got travellers' diarrhoea. I was in bed for a few days while I was away and it took me a while to get over it. I was worried about the baby but it was fine in the end. I did have insurance that covered me, but I still didn't want to go into hospital while I was abroad.

A few years later, we were trying for our third baby and I went to Mauritius with my husband. I found out I was pregnant—about six weeks' gestation—just before we left. While we were in Mauritius, I started to bleed. I was worried about an ectopic pregnancy or a miscarriage because I had already had a miscarriage. I didn't know whether I should try to arrange a scan out there or fly home immediately. Eventually, the bleeding settled and we flew home at the end of the holiday. It was a very difficult time, and I wished I had known that the baby was in the right place and OK.

ADDITIONAL EDUCATIONAL RESOURCES

Resources for health professionals

 $Royal\ College\ of\ Obstetricians\ and\ Gynaecologists.\ Scientific\ Advisory\ Committee\ opinion\ paper\ on\ air\ travel\ and\ pregnancy.\ www.rcog.org.uk/womens-health/clinical-guidance/air-travel-and-pregnancy$

ACOG Committee on Obstetric Practice. ACOG Committee Opinion No 443. Air travel during pregnancy. *Obstet Gynecol* 2009;114:954-5

Royal College of Obstetricians and Gynaecologists. Malaria in pregnancy prevention guidelines. www.rcog.org.uk/prevention-malaria-pregnancy-green-top-54a

 $Health\,Protection\,Agency.\,National\,malaria\,prevention\,guidelines.\,http://www.hpa.org.uk/infections/topics_az/malaria/guidelines.htm$

Centers for Disease Control and Prevention (http://wwwnc.cdc.gov/travel/)—Provides up to date health information for advising those who wish to travel

Medical advisory services for travellers abroad (MASTA) (www.masta.org.uk)—Provides information on whether the travel destination is currently an endemic country:

Resources for pregnant women

Royal College of Obstetricians and Gynaecologists (www.rcog.org.uk/air-travel-and-pregnancy-information-for-you)—Air travel and pregnancy information leaflet

ACOG (www.acog.org/publications/patient_education/bp055.cfm)—Patient education on travel during pregnancy

British Insurance Brokers' Association (BIBA) (www.biba.org.uk)—Provides information on travel insurance for pregnant women

presence of any abnormal symptoms (abdominal pain, bleeding) we advise women to defer travel until the pregnancy location and viability have been confirmed with ultrasound scan and symptoms have settled. If a woman is asymptomatic, many maternity units in the UK do not offer a routine first trimester ultrasound until 11-13 weeks' gestation, and most early pregnancy units do not offer earlier routine scans solely for those considering travelling.

Women consulting after the first trimester

The ACOG considers the second trimester to be the best time to travel.¹⁵ Women who are at increased risk of pre-

term delivery should avoid long haul flights and consider the availability of maternity and neonatal care facilities.²³ Facilities for managing the preterm infant may not be optimal or covered by insurance at the destination, and such facilities are not available on an aircraft. Other serious adverse events in pregnancy (such as major antepartum haemorrhage, severe pre-eclampsia, or cord prolapse) are not common but are difficult to predict; they may be life threatening, especially in the absence of trained personnel and adequate medical facilities. Airlines carry limited resuscitation facilities and often rely on the chance availability of a doctor. Only five of 17 international airlines questioned in 2004 carried delivery kits. 24 A typical leading airline confirmed (2010) that although cabin crew undergo mandatory "pregnancy and emergency childbirth" training, the onboard medical kit contains a delivery pack, one 22 g cannula, one ampoule of ergometrine with oxytocin, and no crystalloid or colloid fluid.

Extended travel abroad and advice on travel insurance

Women should be encouraged to find out about the availability and quality of medical care at their chosen destination, including facilities for mother and baby. If they are travelling for long periods of time they should organise routine antenatal checks abroad. Women should travel with their handheld obstetric notes so that their medical details are readily available to any treating clinician, who can in turn update this information.

A survey of 138 women attending for ultrasound scan at 34 weeks' gestation found that more than a third who had travelled during their pregnancy had done so without adequate insurance. ²⁵ Preterm babies may not be able to be repatriated for some months, and the costs may be substantial. Any woman considering travel while pregnant should take out insurance in the event of medical problems or delivery away from home. Many insurers will cover pregnant women only until 32 weeks' gestation, and women should obtain agreement from their insurer in writing before travel. British women travelling in Europe should get a European Health Insurance Card (EHIC) and carry it at all times; it shows that they are eligible for free or reduced cost emergency medical care but does not replace travel insurance and will not cover the cost of repatriation.

Travel to a malaria endemic country

Risks of acquiring malaria vary considerably. In many parts of sub-Saharan Africa in particular, the average person may get malaria several times a year. The RCOG advises against travel to malaria endemic zones during pregnancy.²⁶ If travel is unavoidable, encourage women to take chemoprophylaxis, which-although not 100% effective-carries a low risk to the fetus, especially in the second and third trimesters, compared with the much higher risks to the pregnancy associated with malarial infection if prophylaxis is not taken. The choice of chemoprophylaxis depends on specific incidence of malaria at the destination and level of drug resistance to Pfalciparum. We advise seeking specialist input for women in the first trimester because of the small theoretical potential for teratogenicity from antimalarial drugs that must be weighed against the substantial risk of acquiring malaria. To avoid bites pregnant women

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Table 2 Travel vaccinations in pregnancy		
Implications in pregnancy	Vaccine	Туре
Considered safe	Hepatitis B	Killed
	Polio (injection)	Killed
	Diphtheria	Toxoid*
	Tetanus	Toxoid
	Immunoglobulins (passive immunity)	Pooled or specific immunoglobulin (for example, measles, rabies, hepatitis A, hepatitis B)
	Influenza†	Killed
Consider if benefit outweighs risk; no evidence of harm	Hepatitis A	Killed
	Japanese encephalitis	Killed
	Rabies	Killed
	Yellow fever‡	Live attenuated
Avoid unless high risk of exposure	Polio (oral)	Live attenuated
	Typhoid (injection)	Killed
Contraindicated	Measles, mumps, and rubella	Live attenuated
	Typhoid (oral)	Live

^{*}Modified or inactivated bacterial toxin.

should always sleep under treated mosquito nets in a malaria endemic area and wear long clothing after dark. A low index of suspicion for a diagnosis of malaria in women who have travelled to endemic areas is vital, and given the high risk to the pregnancy urgent specialist advice is recommended for treatment.

Are travel vaccinations safe in pregnancy?

The risks of vaccination during pregnancy on the developing fetus are unclear. The Centers for Disease Control and Prevention state that there is no evidence of risk from vaccinating pregnant women with inactivated virus, bacterial vaccines, or toxoids.²⁷ It is advised that pregnant women avoid live vaccines, such as yellow fever, because of the small risk of contracting a disease that is potentially harmful to the fetus.²⁸ For yellow fever a letter from a doctor or travel centre stating why vaccination has not been given reduces the risk of pregnant women being turned away or vaccinated on arrival. Inactivated vaccines are generally considered safe, although those associated with febrile reactions (such as oral typhoid) are generally not advised unless the risk is high, because they have been linked with miscarriage.²⁷ Women should seek up to date information from an appropriate travel clinic about vaccination and should be encouraged to avoid disease endemic areas (table 2).

Considerations in the returning pregnant traveller

Routinely ask about recent travel in a pregnant woman who becomes unwell and encourage women to mention recent travel if they become ill on their return. If a travel history is given, have a low threshold for suspecting and looking for thromboembolism and infectious diseases, particularly malaria. A pregnant woman brought up in a malaria endemic area may have malarial anaemia without malaria being visible in the peripheral blood film because of placental sequestration of the malaria parasite. If travel related infection is suspected clinicians should seek specialist advice.

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[†]Follow seasonal guidance from Department of Health (or equivalent).

[#]Ideally after 24 weeks' gestation.