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REVIEW ARTICLE

The pregnant traveller

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ABSTRACT

Travelling during pregnancy has become increasingly common. Many pregnant women travel for pleasure and recreation and a lot of them continue to work and therefore often travel on business, sometimes to areas with poor standards of sanitation and limited access to health care providers. During pregnancy, it is extremely important that a woman has a regular access to maternal health care, also in temporary destinations, especially in areas characterised by harsh environmental conditions, and places where the prevalence of infectious diseases is high. It must be remembered that the course of contagious or parasitic illnesses, such as hepatitis E and malaria, is generally more severe in pregnant travellers, due to pregnancy-related immunosuppression. The assessment of indications and contraindications for the use of mandatory/recommended vaccinations and antimalarial drugs is also very important in pregnant travellers. When pregnant women travel for long term, it is absolutely necessary that they receive prenatal care in a new place of residence. Scheduled maternity care usually begins in week 10–12 of pregnancy, and continues once a month until the 7 month of pregnancy, next every second week until week 36 and then once a week until the delivery.

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Key words: pregnant woman, travelling, tropics

INTRODUCTION

Before going abroad, a pregnant woman should undergo a thorough medical examination. During a pre-travel consultation, a physician should take into account the following factors: all the relevant information regarding the current pregnancy, pre-existing medical conditions (e.g. chronic diseases), the current health status of a pregnant patient as well as the access to health care providers and major risk factors (transmission of infectious diseases) in the destination area [1–3]. It must be remembered that the course of contagious and parasitic illnesses, such as hepatitis E or malaria, is generally more severe in pregnant travellers, due to pregnancy-related immunosuppression [4, 5]. It is also important to appropriately assess the indications and contraindications for the administration of mandatory/recommended vaccinations and the use of antimalarial drugs [6, 7]. Before travelling overseas, pregnant women are recommended to obtain an extended insurance policy covering the costs of treatment and repatriation as well as the costs of care of the newborn (a majority of insurance plans do not account for complications of pregnancy and delivery). They are also advised to check if the air or maritime transport operators are planning any special requirements or procedures applying to pregnant travellers. When travelling abroad expectant mothers must remember to take a copy of their pregnancy medical records including the information on the expected date of delivery, notes on prenatal care and the information on indications and contraindications for travel. They should carry a travel health kit containing all the necessary medications (antiemetic drugs, antacids, medications for the treatment of vaginitis) (Table 1) [1, 8].

When pregnant women travel for long term, it is absolutely necessary that they receive prenatal care in a new place of residence. Scheduled maternity care usually begins in week 10–12 of pregnancy and continues once a month until the 7 month of pregnancy, next it takes place every second week until week 36 and then once a week until the delivery [9].

According to the American Congress of Obstetricians and Gynaecologists, the safest time to travel during preg-

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Table 1. Recommendations for the use of drugs during pregnancy. Source: [8]

Drug name	Recommendations for use during pregnancy
Analgesics, antipyretics	
acetylsalicylic acid (aspirin)	Avoid in the third trimester (risk of premature closure of the *ductus arteriosus*, an increased risk of bleeding)
NSAIDs (ibuprofen, naproxen)	Avoid in the third trimester (the risk of premature closure of the *ductus arteriosus*, possible coagulation disorders; no teratogenic effect)
Antibiotics and antimicrobials	
amoxicillin, amoxicillin/ /clavulanic acid	Safe during pregnancy, the treatment of upper respiratory tract infections (ear infections, pharyngitis, sinusitis)
azithromycin	Safe during pregnancy, recommended for the treatment of bronchitis, pneumonia, gastrointestinal infections caused by enterotoxic *Escherichia coli*, *Campylobacter*, *Salmonella*, *Shigella*
cephalosporins	Safe during pregnancy, recommended for the treatment of upper respiratory tract infections (ear infections, pharyngitis, sinusitis)
clindamycin (oral or external application)	Safe during pregnancy, except for the first trimester; recommended for the treatment of bacterial vaginitis, orally or externally, in the second and third trimester; for the treatment of malaria clindamycin is used in combination with quinine
ciprofloxacin and other quinolones	Avoid during pregnancy; they can be considered for the treatment of severe, life-threatening infections (e.g. anthrax)
doxycycline and other tetracyclines	Avoid in the second half of pregnancy due to possible developmental dental disorders (permanent tooth discoloration)
erythromycin	Safe during pregnancy
penicillin	Safe during pregnancy
nitrofurantoin	First-line therapy for urinary tract infections; avoid in patients with glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency)
Antivirals	
aciclovir	Use only in severe infections
Antidiarrhoeals	
loperamide	Use on demand in severe cases
bismuth compounds	Avoid during pregnancy
Antihistamines	
cetirizine	Safe during pregnancy
loratadine	Safe during pregnancy
Antimalarials	
chloroquine	Safe during pregnancy, used for the prevention and treatment of malaria
mefloquine	Safe during pregnancy, used for the prevention and treatment of malaria
atovaquone/proguanil	Avoid in the first trimester; too little clinical data available to confirm the safety of the drug during pregnancy
doxycycline	Avoid during pregnancy; it can be used in combination with quinine for the treatment of severe, life-threatening infections
quinine	Only recommended for the treatment of life-threatening infections
Antiparasitic	
albendazole	Avoid in the first trimester (teratogenic effect was observed in animal studies); only use in severe cases; if possible, start the treatment after the delivery (avoid while breastfeeding, the active ingredient passes into the breast milk)
metronidazole	Avoid in the first trimester; only use in severe cases
praziquantel	Only use for the treatment of severe schistosomatosis; if possible, start the treatment after the delivery
paromomycin	Low drug absorption; recommended for the treatment of severe tapeworm infections as well as *Entamoeba histolytica* or *Giardia intestinalis* infections
Water disinfectants	
iodine	Avoid during pregnancy (except for short 2/3-week periods); long-term use may result in the formation of foetal goitre and hypothyroidism

nancy is the second trimester. Women generally have the highest risk of miscarriage during the first trimester. In tropical destinations, pregnant women run a higher risk of developing medical conditions associated with the effects of hot climate (high temperature and humidity), e.g. reduced exercise tolerance, increased heart rate associated with an increase in plasma volume and anaemia. Intercontinental travel during pregnancy is especially contraindicated in the following cases [8]:

- chronic diseases: valvular heart disease, severe anaemia, thrombophlebitis;
- obstetric contraindications: patients with a history of pregnancy loss, pre-term labour or ectopic pregnancy; gestosis, arterial hypertension, history of gestational diabetes; imminent abortion or vaginal bleeding during pregnancy; primigravida (first pregnancy at the age > 35 years or < 15 years);
- environmental risk factors: high altitude, transmission food- and water-borne diseases, malaria endemic areas where the resistance of *Plasmodium* to chloroquine has been confirmed, a high risk of the yellow fever transmission, countries where the yellow fever vaccination is mandatory.

TRAVELLING BY PLANE

In general, air travel is considered safe for pregnant women; however, there are certain legal restrictions involved [10]. For instance, expectant mothers may be required by the United States airlines to present a medical certificate stating they are fit for air travel beyond the 36th week of pregnancy (domestic flights) or beyond the 35th week of pregnancy (international flights). Generally, the barometric pressure inside passenger aircrafts is reduced — equivalent to atmospheric pressure at the altitude of 1800–2400 m above sea level. Reduced partial pressure of oxygen decreases foetal oxygenation to a lesser extent than the mother's blood; this is associated with the presence of foetal haemoglobin which has a greater ability to bind oxygen molecules than normal haemoglobin. Owing to this fact, the risk of foetal hypoxia during air travel is low [11, 12]. Due to an increase in plasma volume and the growing morphological demand of the foetus, pregnant women are at a higher risk of developing mild anaemia (iron supplements are recommended in such cases). In more pronounced anaemia (haemoglobin concentration below 8.5 g/dL) air travel is contraindicated. In cases when air travel is necessary, the administration of supplemental oxygen should be considered. Air travel is considered a health risk for pregnant women with sickle-cell anaemia; therefore, they should always attain approval from their obstetrician before travel. The humidity inside airline cabins is low and reaches approximately 8%. Under such conditions, the demand for water in pregnant women increases and is estimated at 3–4 L per day. Regular intake of decaffeinated beverages is necessary to maintain adequate blood flow to the placenta. During long haul flights, when passengers need to remain seated, pregnant women run a higher risk of developing deep vein thrombosis (DVT), which is associated with the effects of sex hormones, compression of blood vessels by the enlarged uterus and the impairment of the venous blood flow [13]. Thus, it is very important that pregnant women take all the necessary measures to prevent DVT, e.g. take a walk up and down the aisle every hour, perform isometric exercise of the lower limbs while seated or wear compression stockings [14]. Although acetylsalicylic acid (aspirin) exhibits antithrombotic effects, it is not recommended in pregnancy, especially in the last trimester due to an elevated risk of bleeding and its teratogenic effects. Pregnant women with a history of thromboembolism or those genetically predisposed to such conditions, should contact their obstetrician before travelling by plane [8].

TRAVELLING BY SHIP

Pregnant women going on a multiple-day cruise should obtain all the necessary information regarding medical assistance available on board (the presence of trained medical personnel, specialist equipment, emergency evacuation procedures). They also need to keep in mind that treatment options for motion sickness are limited during pregnancy (a popular drug used to prevent motion sickness containing dimenhydrinate is contraindicated during pregnancy and in breastfeeding mothers) [15].

VACCINATIONS

Vaccinations are contraindicated during the first trimester of pregnancy, i.e. when the foetus is most vulnerable to damage [16]. Generally, women are recommended to receive all necessary vaccinations before they get pregnant (consciously planned motherhood). With only a few exceptions, live vaccines are contraindicated during all three trimesters of pregnancy (Table 2). The vaccination against yellow fever should only be taken if a woman is travelling to areas where the risk of the disease transmission is particularly high [17]. Pregnant women can abstain from vaccination against yellow fever if they travel to areas where the risk of transmission is low [1]. On such occasions, they may be asked by border guards to present a certificate of pregnancy before they can enter a country which normally requires the International Certificate of Vaccination from international travellers. Similar recommendations on the use of live vaccines apply to breastfeeding women. Research studies have demonstrated that the active ingredient present in the yellow fever vaccine penetrates into breast milk [8].

Table 2. Recommendations for vaccinations during pregnancy. Source: [8]

Vaccination against disease	Recommendations for use
Diphtheria	No contraindications for use
Tetanus	No contraindications for use
Pertussis	No contraindications for use
Hepatitis A	Vaccination is only recommended for women at a high risk of infection; no safety data is available on the use of the vaccine during pregnancy
Hepatitis B	Vaccination is only recommended for women at a high risk of infection
Typhoid fever	Vaccination with live attenuated oral vaccine is contraindicated; a polysaccharide vaccine can be used in women travelling to disease endemic areas
Cholera	Vaccination is not recommended during pregnancy; no safety data is available on the use of the vaccine during pregnancy
Poliomyelitis	Vaccination with live attenuated oral vaccine (OPV) is contraindicated in pregnant women who have not completed the primary vaccination course; inactivated polio vaccine (IPV), used as a booster, is safer than OPV
Meningococcal disease	No safety data is available on the use of conjugated vaccine during pregnancy; polysaccharide vaccines can only be used if there is a high risk of infection
Rabies	Pre-exposure vaccination is only recommended for women at a high risk of infection; post-exposure vaccination is recommended during pregnancy
Yellow fever	Vaccination is only recommended for women at a high risk of infection; when travelling to countries with a low risk of transmission pregnant women can abstain from vaccination, instead, they will be required by border guards to present a certificate of pregnancy before they can enter the country
Japanese encephalitis	Vaccination is only recommended for women at a high risk of infection; no safety data is available on the use of the vaccine during pregnancy
Tick-borne encephalitis	Vaccination is not recommended during pregnancy
Measles, Mumps, Rubella	Vaccination is contraindicated during pregnancy and three months after giving birth
Varicella	Vaccination is contraindicated during pregnancy

MALARIA CHEMOPROPHYLAXIS

Malaria is particularly dangerous for a pregnant woman and her unborn child [18]. If pregnant women need to travel to a malaria endemic destination, they should take all the necessary precautions to avoid disease transmission. Women should avoid becoming pregnant while taking antimalarial drugs as well as after the discontinuation of treatment (1 week for doxycycline, 3 weeks for atovaquone/proguanil and 3 months for mefloquine). There are no contraindications for the use of antimalarials in pregnant women travelling to areas with low-to-moderate risk of malaria transmission (Table 3), i.e. destinations where insect repellents and mosquito nets are recommended preventive measures (the 1st stratum), areas where insect repellents, mosquito nets and chloroquine are necessary (the 2nd stratum) and areas where insect repellents, mosquito nets and chloroquine + proguanil are required (the 3rd stratum). In destinations where the risk of malaria transmission is the highest (the 4th stratum), pregnant travellers are recommended to receive mefloquine but it can only be taken during the 2nd and 3rd trimesters (Table 4) [15]. Doxycycline is contraindicated during the whole pregnancy. There is little clinical data on the clinical safety of atovaquone/proguanil. As regards prevention against insect bites, there are no medical contraindications for the use of repellents containing N,N-diethyl-*meta*-toluamide (DEET) during pregnancy [19]. Clinical studies into products containing DEET at a concentration of max. 35%, e.g. Permethrin, showed no adverse events in pregnant women. Likewise, no adverse effects or developmental disorders were observed in newborns and infants whose mothers had been using DEET-containing repellents during pregnancy in the first 12 months after birth [20].

TREATMENT OF MALARIA

In pregnant women diagnosed with uncomplicated malaria the following drug regimens are recommended: during the first trimester: quinine + clindamycin continued for 7 days; during the second and third trimesters: quinine + clindamycin or artesunate + clindamycin continued for 7 days. Severe malaria in pregnant women should be treated with quinine + clindamycin or artesunate + clindamycin during the first trimester (Table 5), and with artesunate in the second and third trimesters. Chloroquine is recommended for the treatment of *P. vivax* infections, unless chloroquine resistance has been observed. Primaquine, used to prevent the recurrence of *P. vivax* and *P. ovale* infections, is contrain-

Table 3. Type of prevention depending on the risk of malaria. Source: [15]

Risk stratum	Risk of malaria transmission	Recommended prevention
1st stratum	Limited risk of malaria transmission	Repellents, mosquito nets
2nd stratum	Risk of *P. vivax* transmission only; *P. falciparum* susceptible to chloroquine	Repellents, mosquito nets, chloroquine
3rd stratum	Risk of both *P. vivax* and *P. falciparum* transmission; resistance to chloroquine (Nepal, Sri Lanka, Tajikistan, certain regions of Colombia and India)	Repellents, mosquito nets, chloroquine + proguanil
4th stratum	High risk of *P. falciparum* transmission + high antimalarial drug resistance; Medium/low risk of *P. falciparum* transmission + high antimalarial drug resistance In areas with low risk of *P. falciparum* transmission combined use of repellents and stand-by emergency treatment can be considered	Repellents, mosquito nets mefloquine

Table 4. Drugs used for malaria chemoprophylaxis. Source: [15]

Drug name	Dosage regimen	Duration of chemoprophylaxis	Notes
chloroquine	1 × weekly adults: 300 mg	Start 1week before departure, 1 × weekly during travel, continue for 4 weeks after return	Contraindications: epilepsy, psoriasis
chloroquine/ /proguanil	1 × daily > 50 kg bw: 100 mg/200 mg	Start 1 day before departure, 1 × daily during travel, continue for 28 days after return	Contraindications: epilepsy, psoriasis
mefloquine	1 × weekly adults: 250 mg	Start 1 week before departure, 1 × weekly during travel, continue for 4 weeks after return	Increased serum drug concentration in patients treated with ampicillin, tetracyclines and/or metoclopramide Possible neuropsychiatric adverse reactions

Table 5. Drugs used for the treatment of malaria. Source: [15]

Drug name	Dosage regimen
quinine + clindamycin	8 mg/kg bw every 8 h for 7 days + < 60 kg bw: 5 mg/kg bw 4 times a day for 7 days > 60 kg bw: 300 mg 4 times a day for 7 days
artesunate + clindamycin	2 mg/kg bw artesunate once daily for 7 days + 10 mg/kg bw clindamycin twice daily for 7 days
chloroquine	25 mg/kg bw daily divided in 3 doses (10 mg/kg, 10 mg/kg and 5 mg/kg) for 3 consecutive days (it is not to be used in *P. falciparum* infections)
artesunate (severe malaria)	2.4 mg/kg bw IV or IM 0 h (dose 1), 12 h (dose 2), 24 h (dose 3), then once daily
quinine (severe malaria)	20 mg/kg bw IV or IM in 3 doses administered every 8 h (initial dose); next: 10 mg/kg bw IM in 3 doses administered every 8 h; note: in case of IV administration the dose cannot exceed 5 mg/kg bw per hour

dicated for use in pregnant women. There is limited clinical data on the safety of other malaria treatment regimens in pregnant women (artemether/lumefantrine, atovaquone/ /proguanil or dihydroartemisinin/piperaquine) [15].

PREVENTION OF FOOD- AND WATER-BORNE INFECTIONS

When travelling abroad, especially to places lacking adequate sanitation, pregnant women should take all the necessary precautions to prevent transmission of food and waterborne diseases. They should never purchase or consume foods or drinks from local street vendors because it is impossible to check their quality (origin, storage, heat-processing). If symptoms of a food or waterborne infection do occur (diarrhoea, abdominal pain, fever) and medical treatment is necessary, it must be remembered that not all medications are safe during pregnancy. Fever and dehydration, which are common in traveller's diarrhoea, can impair placental blood flow and thus can have a negative effect on foetal development. It is particularly important

Table 6. Travel-related infectious diseases, their risk for foetus, and recommended preventive measures. Source: [23]

Disease	Risk to foetus	Preventive measures
Dengue fever	Acute febrile illness	Insect avoidance
Japanese encephalitis	Encephalitis and seizures	Pre-pregnancy vaccination, insect avoidance
Leishmaniasis	Cutaneous or visceral leishmaniasis	Insect avoidance
Hepatitis A	Hepatitis	Pre-pregnancy vaccination, careful selection of food and water
Typhoid fever	Chorioamninitis, spontaneous abortion, neonatal sepsis	Vaccination, careful selection of food and water
Toxoplasmosis	Chorioretinal lesions, learning disabilities	Avoidance of undercooked meats and contact with animal faeces
Rubella	Deafness, cataracts, cardiac defects, mental retardation	Pre-pregnancy vaccination, proper hand washing
HIV	Congenital and perinatal HIV infection	Avoidance of body fluids, blood transfusions, and drug injections
Hepatitis B	Hepatitis	Pre-pregnancy vaccination, avoidance of body fluids, blood transfusions and drug injections
Hepatitis C	Hepatitis	Avoidance of body fluids, blood transfusions and drug injections

that pregnant travellers take appropriate preventive measures against infectious and invasive diseases affecting the gastrointestinal system, because reduced stomach acidity during pregnancy is associated with increased susceptibility of the gastric mucosa to pathogens. Toxoplasmosis, listeriosis and hepatitis E are particularly dangerous to expectant mothers and their unborn children [9]. It is estimated that 3 of 1000 newborns show signs of congenital toxoplasmosis. The risk for the foetus is especially high if the infection develops during the third trimester of pregnancy. Nearly 50% of newborns affected by toxoplasmosis have symptoms of the disease as early as at birth. Severe complications, including mental impairment, cerebral palsy, deafness and blindness are observed in 5–6% of children with congenital toxoplasmosis. In order to reduce the risk of toxoplasmosis pregnant women should avoid raw or undercooked meat as well as contact with potentially infected cat's faeces, e.g. while cleaning a cat's litter [9]. Also the *Listeria* infection is dangerous for pregnant women. It may be the cause of miscarriage, stillbirth or pre-term delivery. *Listeria* is bacteria found in unpasteurised milk and cheeses, such as feta, Brie or Camembert; therefore, expecting mothers should avoid eating soft cheeses, especially if they had been manufactured in countries with no or little supervision over food production. Hepatitis E, usually transmitted through the faecal-oral route, is caused by the contamination of water supplies with excrement. The disease poses a great risk for pregnant women and can lead to serious health problems including the death of both the mother and her unborn child. In non-pregnant women, the prevalence of acute hepatitis E infection is less than 1%; in pregnant women, however, especially during the third trimester, a HEV infection may develop into fulminant hepatitis with mortality rate reaching 20–30% [21]. A vaccine preventing hepatitis E is not yet available but is currently under clinical trials. Expectant mothers are not recommended to travel to areas where hepatitis E is endemic, especially to the Indian Subcontinent [15].

PREVENTION OF THE ZIKA VIRUS INFECTION

The symptoms of a Zika virus (ZIKV) infection in pregnant women are usually mild, but the virus itself can cause foetal microcephaly and other congenital abnormalities. For this reason, the Centres for Disease Control and Prevention (CDC) recommend pregnant women not travel to areas where ZIKV is present and to take precautions to avoid sexual transmission of the virus (men are recommended to use condoms for a period of 6 months after exposure /return from ZIKV endemic areas; women are advised to avoid getting pregnant during travel and to wait at least 2 months before trying to conceive after returning from endemic region). If a pregnant woman must, for any reason, travel to a Zika endemic country, she must strictly observe preventive measures against mosquito bites [22]. The most current list of countries where ZIKV transmission is present is available at the www.cdc.gov/travel website. Guidance for pregnant women can be found at the CDC Zika website (www.cdc.gov/zika/pregnancy/index.html) [1].

PREVENTION OF OTHER INFECTIOUS DISEASES

Information about prevention of other infectious diseases is presented in Table 6 [23].

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