Travel and pregnancy: an infectious diseases perspective

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Summary: Increasing numbers of women are choosing to travel during pregnancy. In the presence of an altered immune state, exposure to certain microbes can be particularly harmful. We have undertaken a review of the literature in order to provide strategies to minimize the infectious disease risks of pregnant travel. Included is a discussion of common immunizing agents and their safety in pregnancy.

Keywords: travel, pregnancy, infection, immunization, vaccination

INTRODUCTION

Although travel is now commonplace at all stages of pregnancy, it is not without hazard. In the case of infectious risks, it is well recognized that the response to infection during pregnancy is altered with a number of infections carrying higher morbidity and mortality. The precise mechanisms underlying the unique immunological changes of pregnancy are unclear. Rather than viewing the fetus as a bystander in an immune suppressed host, recent paradigms of immune regulation suggest a high degree of interaction within the maternal–fetal–placental unit.¹ Unfortunately, once severe infection is established, changes in cardiac, respiratory and renal physiology can compound to limit the capacity of the pregnant woman to compensate for acute illness.²

As a general rule, travel is best undertaken in the second trimester when the mother feels well and the likelihood of spontaneous miscarriage and preterm labour is lower.³

In attempting to reduce the risk of infection in pregnancy, it is important to consider the infectious diseases epidemiology of the proposed travel destination. In many cases, vaccines or chemoprophylaxis are available and used in combination with practical measures, can enable safer travel at any gestation.

IMPORTANT TRAVEL-ASSOCIATED INFECTIONS

As they generally carry a worse prognosis in pregnancy, several infections warrant special attention. Of note are malaria, influenza, hepatitis E virus and listeria. Travellers diarrhoea is also discussed given its frequency and difficulties associated with antimicrobial use in pregnancy. While this list is not intended to be exhaustive, the preventive advice presented is also applicable to a wide range of travel-associated infections.

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MALARIA

Malaria continues to exact a significant toll in tropical developing nations. With approximately 283 million cases of malaria worldwide in 2008, it is estimated to account for close to a million deaths per annum.⁴

Four species of *Plasmodium* parasite are the main causes of human malaria (*P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*).

Transmission is via an arthropod vector, the anopheles mosquito and occasionally vertically, via blood transfusion, organ transplantation or shared needles.

Anopheles mosquitoes are most active at dawn and dusk with the female anopheles injecting the plasmodium parasite into the human bloodstream during a blood meal. Parasites subsequently multiply in the liver and infect red blood cells.

The gold standard for diagnosis remains thick and thin blood films to identify the presence of parasites within red blood cells. Rapid diagnostic tests such as the immunochromatographic assays (ICT) are also very commonly used for diagnostic screening but may give false-negative results in non-immune patients with low or very high parasitaemias.⁵

Symptom onset varies depending on the *Plasmodium* species but illness typically manifests as fever, headache and vomiting. Women from non-malarious areas have low premunition and are at particularly high risk of complications both in themselves and in the fetus.⁶

Death from malaria occurs as a result of multiorgan failure culminating in coma, massive haemolysis, adult respiratory failure and acute renal failure.

Placental malaria can cause intrauterine growth restriction, intrauterine death, preterm delivery and neonatal mortality.⁷ It is the leading cause of maternal mortality directly and indirectly in many countries in Africa.⁸

Thus, suspected malaria in a pregnant woman should always be treated as a medical emergency.

STRATEGIES FOR PREVENTING MALARIA

Wherever possible pregnant women should avoid travel to areas of high malaria endemicity. When travel cannot be

deferred, chemoprophylaxis can be offered with the caveat that no regimen is 100% effective.

Susceptibility of plasmodium species to the available chemoprophylactic regimens varies. The traditional treatment dichotomy has been between chloroquine-sensitive and chloroquine-resistant *Plasmodium* species. A number of Internet resources are helpful in determining the likely susceptibility profile of *Plasmodium* within a particular geographic region.⁹ Chloroquine resistance is increasing, particularly in Asia; thus depending on regional epidemiology and patient factors mefloquine is increasingly being employed and recommended as a first-line agent in the second and third trimesters. While there are limited data for the use of mefloquine in the first trimester, its use may be justified where there is high risk of chloroquine-resistant falciparum malaria.⁹ While doxycycline is still employed for prophylaxis in chloroquine-resistant areas it is best avoided in pregnancy due to the risk of fetal tooth discoloration.

Table 1 summarizes the experience with current options in pregnancy.

Other methods of malaria risk reduction are targeted towards mosquito bite avoidance.

Pregnant women should be advised to^{3,9,10}

- Stay indoors at dusk and dawn;
- Exercise extra caution overnight as most of the bites occur after dark;
- When outdoors at night, wear light-coloured clothing including long sleeved pants and sleeves, socks and covered shoes;
- Reside in well-constructed housing preferably with air-conditioning and/or screens;
- Use insect repellants containing 50% DEET sparingly but as needed.^a In humid environments more frequent application is required;⁹
- Use pyrethrum-containing house sprays or coils indoors as required;
- Sleep under permethrin-impregnated bed nets.

Even in the absence of chemoprophylaxis, these barrier methods for malaria prevention are highly effective and should be employed in any malarious region.

INFLUENZA

Retrospective analyses across multiple influenza outbreaks have demonstrated that pregnant women are at greatly increased risk of morbidity and mortality, particularly in the second and third trimesters.^{13,14} The 2009 H1N1 influenza pandemic was no exception, with data suggesting a four-fold increase in hospital admission for pregnant women when compared with the general population.¹⁵ A retrospective Australian study found an excessively high rate of maternal complications, preterm labour and fetal/maternal mortality.¹⁶

In spite of public health campaigns and evidence supporting the safety and efficacy of inactivated influenza vaccination, vaccine uptake was low during the pandemic.¹⁷ For example

in the USA only about 20% of adults were vaccinated against H1N1.¹⁸ Despite the increased risk of complications from influenza and the specific vaccination recommendation, vaccination rates have been found to be even poorer in pregnant women.¹⁹ This is generally attributed to a number of factors. In particular, concerns of both pregnant women and health practitioners regarding the safety of vaccination in pregnancy, underestimation of the risk that influenza poses in pregnancy and vaccination not being actively sought or encouraged in obstetric care settings.^{20,21}

Currently both the Advisory Committee on Immunization Practices (ACIP) and the American College of Obstetricians and Gynaecologists (ACOG) recommend that *all women who are or will be pregnant during the influenza season^b* should receive inactivated influenza vaccine regardless of gestational age.²² Influenza vaccination during pregnancy also has the added benefit of conferring passive immunity to the neonate.

Aside from immunization the following are advisable during the flu season:

- Regular hand washing;
- Avoiding people with symptoms of upper respiratory tract infection symptoms, i.e. coughing, sneezing;
- Avoiding large crowded gatherings.

Face masks were also employed en masse in some countries.²³ While face masks can reduce the risk of transmission, efficacy varies depending on the type of mask used.

Should corrhylal symptoms or fever occur while travelling, early medical review is imperative as early diagnosis and institution of antiviral therapy facilitates improves maternal and fetal outcomes.

HEPATITIS E

Hepatitis E virus (HEV) remains the most common cause of clinical acute viral hepatitis in the developing world.⁷ In non-pregnant individuals hepatitis E is usually self-limiting with a low mortality of less than 0.1%. Unfortunately, the pregnant cohort are at increased risk of death 5–25% and vertical transmission can result in miscarriage, stillbirths, neonatal deaths and hepatic injury.²⁵

Four major routes of transmission have been identified; faecally contaminated water, consumption of the undercooked meat of infected animals, blood-borne and vertical transmission. With an incubation period of 15–45 days the classical clinical presentation is of fever, nausea, vomiting, jaundice, dark urine, tender hepatomegaly and raised hepatic enzymes.²⁶

Diagnosis can be established by means of blood PCR to identify HEV RNA or serology.

Two trials of hepatitis E vaccine have shown encouraging results in terms of safety and efficacy but unfortunately industry impetus to get either vaccine to market has waned.²⁷ In the absence of a vaccine, preventive efforts are reliant on stringent food and water hygiene.

Key measures for preventing hepatitis E include:²⁹

- Hand hygiene before and after eating and toileting;

^aDEET (*N,N*-diethyl-*meta*-toluamide) is the active ingredient in many over-the-counter insect repellents. Cases of DEET toxicity have been reported when used in high doses but in spite of its widespread use since the 1950s no known fetal risks have been identified.

^bThe influenza season occurs in the colder months of both the Northern and Southern hemispheres. e.g. USA October to May versus Australia April to October.

Table 1 A guide to malaria chemoprophylaxis in pregnancy^{9–12}

	Options	Safety in pregnancy	Dosing regimen	Adverse effects/precautions	Comments
Chloroquine-sensitive <i>Plasmodium</i> species	Chloroquine phosphate	Not known to cause any adverse fetal or pregnancy outcomes	Chloroquine 310 mg base (=2 tablets of chloroquine phosphate 250 mg) orally, once weekly Starting 1 week before entering, and continuing until 4 weeks after leaving the malarious area	Exacerbation of psoriasis	Primaquine contraindicated due to the risk of precipitating haemolytic anemia in a fetus with G6PD deficiency
Chloroquine-resistant <i>Plasmodium</i> species	Mefloquine*	Data suggest no increase in adverse fetal events or pregnancy outcome when taken at prophylactic doses in the 2nd or 3rd trimester. Limited data suggest it is also safe in the first trimester	Mefloquine 250 mg orally, once weekly (starting 2–3 weeks before entering, and continuing until 4 weeks after leaving the malarious area)	Contraindicated in patients with active depression, a recent history of depression, generalized anxiety disorder, psychosis, schizophrenia, other major psychiatric disorders or seizure disorders Use cautiously in people with psychiatric disturbances or a previous history of depression. Avoid in patients with cardiac conduction abnormalities.	Atovaquone proguanil is not currently recommended for use in pregnancy due to insufficient data on its safety Doxycycline is contraindicated due to the potential risk of fetal tooth discoloration when used after the first trimester

*Some areas of southeast Asia now report mefloquine resistance. Where mefloquine cannot be used and prophylaxis is deemed essential consult local travel health agency

- Avoiding water and ice of unknown purity;
- Avoiding uncooked shellfish;
- Avoiding uncooked fruits or vegetables that have not been peeled or prepared by the traveller;
- Where water purity is not guaranteed, boil water or treat it with iodine or chlorine preparations and use a water filter.

Treatment for hepatitis E virus is supportive and no anti-virals have been shown to alter the disease course.

LISTERIA

Listeria monocytogenes is a well-recognized bacterial cause of fetal death *in utero*. Fetal death is attributable to fetal bacteraemia as well as placental dysfunction.³⁰ *Listeria* is spread to the fetus haematogenously following ingestion of contaminated food products by the mother. As well as being widespread in soil, *listeria* forms part of the normal faecal flora of many mammals. Thus many foods are commonly contaminated with *listeria* and asymptomatic infection is probably a common occurrence in the general population. However, pregnant women have an estimated 17-fold increased risk of listerial bacteraemia³¹ in which case infection typically manifests as febrile gastroenteritis, sepsis syndrome or meningitis.³²

Dietary recommendations for preventing listeriosis in pregnancy include:³³

- Thorough cooking of raw food from animal sources;
- Washing of raw vegetables prior to consumption;
- Avoiding consumption of products containing unpasteurised dairy products;
- Avoiding soft cheeses (e.g. feta, brie, camembert);
- Thorough re-heating of leftover food;
- Avoidance of foods from delicatessen counters and buffets.

Maintaining a limited stock of emergency food and water supplies is advisable.

Diagnosis hinges on culture of *L. monocytogenes* from normally sterile specimens such as CSF, blood, joint fluid. Unfortunately, serology has not been shown to be of use in acute diagnosis. Intravenous Ampicillin remains the preferred antibacterial agent for listeriosis.

TRAVELLERS' DIARRHOEA

Diarrhoea remains one of the most common illnesses affecting international travellers and is estimated to affect 20–60% of travellers visiting low-income destinations.³³

Enteric bacteria are generally considered the most frequent aetiological agents, in particular *Escherichia coli*, *Campylobacter*, *Salmonella* and *shigella* species. Of the viral agents, Norovirus and Rotavirus predominate while *Giardia intestinalis* and

Table 2 Immunoglobulins^{38,39}

Immunizing agent	Mechanism of action	Examples	Risks/comments
Antibodies (Immunoglobulins)	<ul style="list-style-type: none"> • Confer passive immunity • Provide temporary protection • Effective within hours • Short lived duration of action (weeks to months) • IgG preparations cross the placenta and can provide fetal protection also 	CMV IgG Hepatitis A IgG Hepatitis B IgG Rabies IgG Tetanus IgG Varicella zoster IgG	No known risks exist to the fetus from passive immunization using immunoglobulin preparations May be used for pre- and postexposure prophylaxis

Table 3 Types of vaccines^{7,38}

Immunizing agent	Mechanism of action	Types of vaccines	Examples	Risks/comments
Vaccines	<ul style="list-style-type: none"> Active immunity Evoke the host immune system to generate endogenous protection Can take weeks to months to take effect Prolonged duration of effect (years) Provide fetal protection 	Live attenuated <ul style="list-style-type: none"> Organisms retain the capacity to multiply at a low level in the recipient but have had their virulent capacity disabled. Single doses generally result in lifelong immunity 	Measles Mumps Rubella Varicella Polio (Sabin) Cholera Yellow fever BCG Small pox Typhoid	Live vaccines have a theoretical risk of reactivation to the virulent form
		Inactivated/killed <ul style="list-style-type: none"> Organisms are not able to replicate in the recipient therefore not capable of causing true disease. Frequently require repeat dosing, i.e. annual to maintain immunity 	Influenza Hepatitis A	
		Toxoid <ul style="list-style-type: none"> Inactivated toxic compounds that enable the recipient to generate antibodies against native microbial toxins 	Tetanus Diphtheria	
		Subunit <ul style="list-style-type: none"> Employs only a small protein subunit of an organism as opposed to the whole 	Hepatitis B	
		Conjugate <ul style="list-style-type: none"> Combines weakly immunogenic microbial proteins, e.g. membrane polysaccharides with more immunogenic compounds 	HiB	
		Recombinant <ul style="list-style-type: none"> Generated by combining the replicative machinery and antigens of two different organisms. Not capable of causing true infection 	Hepatitis B	

Cryptosporidium account for the majority of parasite-associated infections.³³

The clinical syndrome usually consists of a self-limiting diarrhoeal illness which resolves within seven days. However, symptoms do vary depending on the causative agent. For example, infection with enterotoxigenic *E. coli* classically presents as short-lived watery stools with abdominal cramping and nausea whereas Giardiasis can be protracted, causing chronic malabsorption and weight loss.

In terms of disease prevention, destination country and choice of eating establishment have been identified as key determinants of risk.³⁵ Notably most disease burden occurs in South Asia, Africa and Latin America. Thus when travelling to these regions, avoidance of specific eating environments such as street vendors is prudent. Cooked foods that have been left at room temperature in warm environments serve as an ideal medium for bacterial growth.³³ The dietary precautions outlined with hepatitis E and listeria also apply.

Treatment of travellers' diarrhoea in pregnancy is vexed by the potential fetal risks of commonly used antimicrobial agents. The fluoroquinolones (norfloxacin, ciprofloxacin, ofloxacin, levofloxacin) are currently designated category C by the US Federal Drug Agency (FDA),^c i.e. there are inadequate data on fluoroquinolone use in pregnant women, although

animal studies have shown evidence of postexposure fetal anomaly, in particular, arthropathies. Therefore, potential benefits should be weighed against risks. Another common treatment alternative is the macrolide antibiotic, azithromycin. Azithromycin is designated as FDA category B, i.e. there is no documented risk in animal studies but there are insufficient data to preclude fetal risk in pregnancy.

Thus irrespective of the agent chosen to treat travellers' diarrhoea in pregnancy, a discussion should be entered into regarding the safety of each. In our clinical practice, we use azithromycin in preference to quinolones in pregnancy.

IMMUNIZATIONS IN PREGNANCY

Vaccination is often a source of angst for both pregnant women and health practitioners. Much consternation and confusion surrounds the use of live bacterial and viral vaccines. These have a theoretical risk of causing active infection and vertical transmission to the fetus. However, in cases where live vaccine is administered inadvertently, e.g. Measles-Mumps-Rubella vaccine this *should not* be grounds for termination.²⁹ The controversy over a suspected link between thiomersal, a mercury-based preservative agent, and autism has also fed into community concerns about vaccine safety. The current scientific consensus is that there is no sound basis for an association between thiomersal and childhood neurodevelopmental abnormalities.³⁴ Nonetheless, the general lack of data in the pregnant cohort dictates that any decision to immunize should be based on a judicious risk versus benefit analysis. To avoid any such concerns, whenever

^cRisk stratification tools vary across regions. Specifically, category C FDA drugs are those in which 'animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks'.

Table 4 Guidelines to the use of vaccines in pregnancy^{29,39}

Vaccine	Should be considered if otherwise indicated	Contraindicated during pregnancy	Safety in pregnancy/ comments
Routine			
Hepatitis A	✓		Inactivated virus vaccine – limited data but expected to be low risk to fetus Immunoglobulin – no known risk to fetus
Hepatitis B	✓		Limited data indicate no apparent risk for adverse fetal events. Women who are high risk should be vaccinated.
Influenza (inactivated)	Recommended		Inactivated vaccine recommended for all women who are or will be pregnant during the influenza season as per ACOG and ACIP.
Influenza (LAIV)*		✓	Theoretical risk of reactivation
Measles* Mumps* Rubella*		✓	Theoretical risk of reaction
Meningococcal MCV4			Conjugate vaccine Limited data in pregnancy Recommended in outbreaks
Pneumococcal PPV23 Polysaccharide			No adverse events have been reported after inadvertent vaccination during pregnancy. Women with chronic diseases, smokers and immunosuppressed women should consider vaccination.
Polio (Inactivated Polio Vaccine) Salk	✓		Limited data but no documented adverse effects on pregnant women or fetuses
Polio (Oral Polio Vaccine)* Sabin		✓	Theoretical risk of reactivation
Tetanus-diphtheria (Td)	✓		Toxoid vaccine – no documented evidence of teratogenicity Indicated if no previous complete immunization history OR those with previous single dose Td vaccine in the last 10 years can receive booster Second or third trimester administration preferred
Tetanus-Diphtheria-Pertussis (Tdap)			Limited data If indicated to provide protection against Tetanus, Diphtheria and Pertussis. Limited data Second or third trimester preferred
Varicella*		✓	Risk of reactivation and fetal transmission
Travel			
Anthrax			Consider if benefit outweighs risk
BCG*			Theoretical risk of disseminated infection
Japanese encephalitis			No data. Pregnant women who must travel to an area where the risk is high should be vaccinated when risks are outweighed by the risk of disease
Meningococcal MPSV4 polysaccharide	✓		On the basis of current data pregnancy should not preclude vaccination with MPSV4 if indicated
Rabies	✓		Indications not altered by pregnancy. If risk of exposure to rabies is substantial, pre-exposure prophylaxis may also be indicated
Typhoid			No data have been reported on the use of any of the three typhoid vaccines in pregnancy. Polysaccharide typhoid vaccine is a potential option if risk is high
Vaccinia*		✓	Theoretical risk of reactivation
Yellow fever*			The safety of yellow fever vaccine in pregnancy has not been established If travel to an endemic area with increased risk of exposure is unavoidable then vaccine should be administered If international travel requirements are the only reason for vaccination with low risk of exposure then a waiver letter may be sought
Zoster		✓	Limited data. Manufacturer recommends against using Zostavax in pregnancy

*Live vaccines. ACOG = American College of Obstetricians and Gynaecologists; ACIP = Advisory Committee on Immunization Practices

possible, it is prudent to ensure that vaccination status is up to date in pre-pregnancy.

A basic understanding of the types of immunizing agents available and their constituents aids in guiding rational decision-making. This is particularly true given that a number of options may be available for the purposes of immunizing against a single infectious agent, e.g. hepatitis A. Thus in some instances (if indicated) it may be feasible to provide immediate protection with an immunoglobulin preparation and then perform formal vaccination postpartum.

Serological assessment at baseline also provides an easy means of assessing immune status and obviates unnecessary vaccination.

In counselling pregnant women on their vaccination plans, it is important to remember that many infections such as measles that were previously considered 'eradicated' in the developed world have recrudesced due to falling immunization rates and remain regular occurrences in some developing countries.³⁶ Effort also needs to be made to establish the infectious diseases epidemiology and statutory regulations regarding vaccination in

the proposed travel destination.³⁶ For example, several countries request evidence of yellow fever vaccination prior to entry.

Ideally immunization planning should commence at least 4–6 weeks prior to travel to enable completion of vaccination protocols and where necessary assess for serological response.

Tables 2–4 provide a guide to a comparison between immunoglobulins and vaccines.

CONCLUSION

Travel during pregnancy can lead to infectious disease exposures. In an age of increased access to travel, obstetric care providers will continue to be called upon to assist in managing these risks. This need not require in-depth infectious diseases knowledge but a basic appreciation of disease epidemiology and the fundamentals of immunization and chemoprophylaxis should provide a guide for discussing care options with pregnant women.

There are little data on the use of the new antimalarials in pregnancy, so it is important to assess risk thoroughly and prescribe prophylaxis very prudently in pregnancy if visiting high-risk areas during pregnancy cannot be avoided.

Apart from influenza vaccination, most pretravel vaccinations are best done pre-pregnancy if possible, although many can still be administered during pregnancy if the context warrants it.

Referral to or consultation with a facility familiar with travel health medicine can then enable a thorough assessment and action plan.

Finally, many infectious disease risks can be mitigated with good planning to ensure safer travel at any gestation.

DECLARATIONS

The authors have no conflicts of interest to declare.

REFERENCES

- Mor G, Cardenas I. Review Article: The immune system in pregnancy: a unique complexity. *Am J Reprod Immunol* 2010;**63**:425–33
- Joseph J, Sinha A, Paech M, Walters BNJ. Review Article: Sepsis in pregnancy and early goal-directed therapy. *Obst Med* 2009;**2**:93–9. Last checked 1 April 2011
- See <http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-8/traveling-while-pregnant.aspx>. Last checked 1 April 2011
- See http://www.who.int/gho/mdg/diseases/malaria/situation_trends_mortality/en/index.html. Last checked 31 January 2011
- The Royal College of Obstetricians and Gynaecologists. The diagnosis and treatment of malaria in pregnancy. RCOG Green-top Guideline No. 54B. April 2010
- The Royal College of Obstetricians and Gynaecologists. The prevention of malaria in pregnancy. RCOG Green-top Guideline No. 54A. April 2010
- Mandell GL, Bennett JE, Dolin R, eds. *Principles and Practice of Infectious Diseases*. 7th edn. Philadelphia: Churchill, Livingstone, Elsevier/Jamison, 2010
- Jamison DT, Feachem RG, Makgoba MW, Bos ER, Baingana FK, Hofman KJ, Rogo KO, eds. Malaria. In: *Disease and Mortality in Sub-Saharan Africa*. 2nd edn. Chapter 14. Washington, DC: World Bank, 2006. See <http://www.ncbi.nlm.nih.gov/books/NBK2286/>. Last checked 1 April 2011
- See <http://www.cdc.gov/malaria/map/>. Last checked 1 April 2011
- See <http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/malaria.aspx>. Last checked 1 April 2011
- Jacquerioz FA, Croft AM. Drugs for preventing malaria in travellers. *Cochrane Database Systematic Rev* 2009 Issue 4. See <http://onlinelibrary.wiley.com/o/cochrane/clsysrev/articles/CD006491/frame.html>. Last accessed 1 April 2011
- Antibiotic Expert Group. *Therapeutic Guidelines: Antibiotic Version 14*. Melbourne: Therapeutic guidelines Limited, 2010
- Ahluwalia IB, Jamieson DJ, Rasmussen SA, D'Angelo D, Goodman D, Kim H. Correlates of seasonal influenza vaccine coverage among Pregnant women in Georgia and Rhode Island. *Obstet Gynecol* 2010;**116**:949–55
- Brown CM. Severe influenza A virus (H1N1) infection in pregnancy. *Obstet Gynecol* 2010;**115**:412–4
- Ang LT, Gandhi K, Qin Y-HV. Respiratory failure in pregnant women infected by swine-origin Influenza A H1N1. *Austra. N Z J Obstet Gynaecol* 2010;**50**:294–6
- Hewagama S, Walker SP, Stuart RL, et al. 2009 H1N1 influenza A and pregnancy outcomes in Victoria, Australia. *Clin Infect Dis* 2010;**50**:686–90
- Tamma PD, Steinhoff MC, Orner SB. Influenza infection and vaccination in pregnant women. *Expert rev Respir Med* 2010;**4**:321–8
- Harris KM, Maurer J, Kellerman AL. Influenza vaccine- safe, effective and mistrusted. *N Engl J Med* 2010 Published online Nov 24, 2010. See <http://www.nejm.org/doi/full/10.1056/NEJMp1012333>, also see <http://www.nejm.org/doi/pdf/10.1056/NEJMp1012333>
- White SW, Petersen RW, Quinlivan JA. Pandemic (H1N1) 2009 influenza vaccine uptake in pregnant women entering the 2010 influenza season in Western Australia. *MJA* 2010;**193**:405–7
- Yudin MH, Salaripour M, Sgro M. Pregnant women's knowledge of influenza and the use and safety of the influenza vaccine during pregnancy. *J Obstet Gynaecol Canada* 2009;**31**:120–5
- White SW, Petersen RW, Quinlivan JA. Pandemic H1N1 Influenza 2009 vaccine uptake in pregnant women entering the 2010 influenza season in western Australia. *Med J Australia* 2010;**193**:405–7
- ACOG Committee opinion no 468. American College of Obstetricians and Gynecologists. Influenza Vaccination during pregnancy. *Obstet Gynecol* 2010;**116**:1006–7
- Cowling BJ, Chan KH, Fang VJ, et al. Facemasks and hand hygiene to prevent influenza transmission in households: a cluster randomized trial. *Ann Intern Med* 2009;**151**:437–46
- Navaneethan U, Mojaher MA, Shata MT. Hepatitis E and pregnancy: understanding the pathogenesis. *Liver Int* 2008;**28**:1190–9
- The Lancet. Editorial: Hepatitis E vaccine: why wait? *Lancet* 2010;**376**:845
- Khuroo MS. Hepatitis E virus. *Curr opin Infect Dis* 2008;**21**:539–43
- Basnyat B. Neglected Hepatitis E and typhoid vaccines. *Lancet* 2010;**376**:869
- See <http://www.who.int/mediacentre/factsheets/fs280/en/>. Last checked 1 April 2011
- Center for Diseases Control. Guidelines for Vaccinating pregnant women. See <http://www.cdc.gov/vaccines/pubs/preg-guide.htm> (last checked 28 November 2010)
- McLure EM. Infectious causes of stillbirth: a clinical perspective. *Clin Obstet Gynecol* 2010;**53**:635–45
- Mylonakis E, Hohmann EL, Calderwood SB, Wing EJ. Listeriosis during pregnancy: a case series and review of 222 cases. *Medicine* 2002;**81**:260–9
- Jackson KA, Iwamoto M, Swerdlow D. Pregnancy associated listeriosis. *Epidemiol Infect* 2010;**138**:1503–9
- Hill RD, Ryan ET. Management of travellers' diarrhea. *Bri Med J*. 2008;**337**:863–7
- Federal Drug Administration. See <http://www.fda.gov/BiologicsBloodVaccines/Vaccines/QuestionsaboutVaccines/UCM070430>. Last checked 1 April 2011
- Hill D, Beeching N. Travelers' diarrhea. *Curr Opin Infect Dis* 2010;**23**:481–7
- Omer S, Salmon D, Orenstein W, Dehart M, Halsey N. Vaccine refusal, mandatory immunization, and the risks of vaccine-preventable diseases. *N Engl J Med* 2009;**360**:1981–8
- See <http://wwwnc.cdc.gov/travel/destinations/list.aspx>. Last checked 1 April 2011
- Grabenstein JD. *Immunofacts: Vaccines and Immunologic Drugs*. Missouri: Wolters Kluwer Health, 2007
- Kroger AT, Atkinson WL, Pickering LK. CDC general recommendations on immunizations: recommendations of the Advisory Committee on Immunisation Practices (ACIP). *Morbidity Mortality Weekly Rep* 2006;**55**:32–3

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