

TREATMENT OF COMMON MEDICAL PROBLEMS IN PREGNANCY PART II

- ☐ The majority of medicines are not licensed for use in pregnancy and no drug is safe beyond all doubt in pregnancy
- ☐ Where more than one drug is required, the minimum number of drugs should be prescribed.
- ☐ The lowest effective dose should be used for the shortest possible time.
- ☐ Prescribers should stress the importance of avoiding herbal remedies in pregnancy.
- ☐ The risk of acute disease is often greater than a theoretical drug risk.

It is estimated that 40-90 % of women are exposed to medications during the course of their pregnancy, and 34% of women are medication free in the first trimester.^{2,50,76-81} Drug consumption is higher in pregnant women who engage in risk taking behaviour (e.g. smoking, alcohol, recreational drugs) and varies according to socioeconomic factors such as education, affluence and race.⁷⁷ In one survey, 82% of women received an average of 4 drugs during pregnancy, excluding iron supplements, and 65% of women self-medicated.⁸¹ Moreover, women may tell their GP's of as few as 25% of the OTC preparations they have taken.⁸² Ideally, all drugs should be avoided in the first trimester,^{3,5,8} This recommendation is not always feasible.⁸³ However, with reassurance and non-drug approaches, many women may be able to tolerate their discomfort. Physicians should prescribe in pregnancy where drugs are indicated; indeed failure to prescribe appropriate drug treatment may result in an adverse outcome.⁷⁶ Physicians should stress the importance of avoiding self-medication (especially "natural" herbal remedies). Community pharmacists have a vital role to play in patient education and safe counter-prescribing during pregnancy.

MIGRAINE

Pre-existing migraine tends to worsen during the first trimester but improves thereafter.^{8,75,84-87} **Non-pharmacological approaches** (e.g. bed rest, massage, stress-management, ice-packs and biofeedback) should be tried first. Avoidance of known trigger factors (e.g. chocolate, cheese, red wine) should be advised as well as regular small meals to avoid hypoglycaemia.⁸⁸

Drug treatment, when necessary, should be aimed at acute therapy. Chronic treatment should be avoided. Simple analgesics such as **paracetamol** with or without **codeine**, are not associated with teratogenic risk and should be used first-line.^{8,85} If need be, an **anti-emetic** may be given (see below).⁸⁸ Long-term use of **narcotic** analgesics, should be avoided as this may lead to maternal and neonatal addiction.⁵⁰ Simple analgesics in combination with **caffeine** may be useful.⁸⁶ Caffeine potentiates analgesia. Occasional use of low-dose **aspirin** (75 mg) carries no apparent risk.^{6,89} Regular use of aspirin, or its use in the last 3 months of pregnancy, should be avoided because of the potential for metabolic acidosis, platelet abnormalities, prolonged labour and LBW.^{20,50,84,89} Short-term use of **NSAIDs** is not contra-indicated in early pregnancy,^{51,86} but should be avoided in the third trimester due to the risk of premature closure of the ductus arteriosus.^{6,8,86} OTC use of NSAIDs is not recommended.

Severe acute attacks may require hospitalisation for treatment and rehydration.^{75,86} Migraine prophylaxis may be indicated where more than 3-4 acute attacks occur per month, but should only be used as a last resort.⁸⁶ **Propranolol** is the prophylactic drug of choice, but has been associated with IUGR.^{8,18,86} **Ergotamine** and its derivatives are contra-indicated because of their vasoconstrictor and oxytocic effects.^{86,89} **Sumatriptan** should be avoided because safety data in human pregnancy is lacking.⁸

NAUSEA AND VOMITING

Nausea and vomiting are the most common and troublesome symptoms of early pregnancy. Estimated incidences range from 50-90% and symptoms are often considered diagnostic of pregnancy.^{18,53,90-93} It is usually self-limiting and in many cases, may be managed supportively with **reassurance** and **dietary advice**.^{6,18,53} Patients should be encouraged to eat small meals, rich in carbohydrate and low in fat and to avoid drinking large volumes in the morning.^{17,53,90,94,95} A dry carbohydrate-rich snack early in the morning may be particularly helpful.⁵⁴ Anti-emetic therapy may be required in patients with intractable symptoms, unresponsive to these measures.

Treatment of vomiting is especially important in women on maintenance drug therapy (eg antiepileptics) as vomiting will compromise drug absorption and affect disease control.

The antihistamines **cyclizine**, **meclozine** and **promethazine theoclate** are widely prescribed in pregnancy as first-line agents.^{17,18,53,94} **Prochlorperazine** is no longer as widely prescribed due to reports of cardiovascular abnormalities.^{17,18,48,94} Prochlorperazine suppositories may however be useful in severe vomiting.^{94,96} **Metoclopramide** has been used for years with no known teratogenic effects.^{94,96,97} However, metoclopramide may precipitate extrapyramidal effects in young women (especially in under 25's) and should be used second-line to antihistamines. **Pyridoxine** (vitamin B6) is safe and has proved effective.^{18,92,96} It is used as first-line treatment in some countries.⁹⁶

Hyperemesis gravidarum is characterised by intractable vomiting associated with fluid, electrolyte and nutritional depletion.⁹⁸⁻¹⁰⁷ There may be associated thyroid and liver dysfunction.^{104,105} Patients must be hospitalised for fluid, electrolyte and nutritional supplementation. Psychotherapy may be helpful. Parenteral antiemetics are recommended. Intravenous steroids are sometimes indicated.^{102,103} Use of ondansetron has proved effective without teratogenic effects in anecdotal cases.^{106,107} In severe cases, early delivery may be indicated. Hyperemesis gravidarum is more common in primigravidae.¹⁰¹

PRURITUS

Generalised itching is common in pregnancy. When present in the absence of a rash during the third trimester pregnancy cholestasis should be suspected and a liver profile performed. Referral for specialist care and monitoring of fetal health is essential. Mild forms of pregnancy cholestasis may respond to topical antipruritics (e.g. **calamine** lotion). Otherwise, **cholestyramine** (Questran) 4g tds should be prescribed.¹⁰⁸ Cholestyramine sequesters the bile salts causing the itch. However, it impairs the absorption of the fat-soluble vitamins D and K, and so **vitamin supplementation** is advised. **Ursodeoxycholic acid** (50mg/kg/day for 20 days) and **dexamethasone** (12mg daily for 7 days, reducing over 3 days) have also been used effectively.¹⁰⁹ Cholestatic pruritus is associated with an increased incidence of stillbirths, prematurity and fetal distress.¹⁰⁹ Early delivery may be indicated. Combined oral contraceptives are best avoided in women with a history of pregnancy cholestasis.¹⁰⁹

Use of **emollient bath additives** (with cornstarch or oats), **moisturising creams** and **talcs** twice daily is recommended for other mild forms of pruritus. Irritating soaps and foam baths should be avoided. Where topical treatments are insufficient, a systemic antihistamine should be prescribed for 10 days.¹⁰⁸ **Chlorpheniramine** or **hydroxyzine** are preferable and are safe to use during the first trimester. When taken at night, their sedative properties may alleviate insomnia due to intense itch. Where antihistamines are ineffective, a short-acting benzodiazepine may be effective for short-term use (< 1 week).¹⁰⁸ **Corticosteroids**, topical or oral, are not recommended for the management of pruritus without lesions or obvious cause (e.g. eczema). Atopic eczema generally improves during pregnancy.¹⁸

SCABIES AND LICE

Scabies and lice occur commonly in pregnancy, especially where there are other school-going children in the family. **Malathion** (Prioderm, Derbac M) is the treatment of choice for scabies and lice in pregnancy.⁵ There is less experience with the use of **permethrin** (Lyclear). Although no adverse effects have been reported to date, permethrin should be used with caution in pregnancy.¹¹⁰ **Lindane** is contra-indicated. In animal studies, high doses of lindane have been associated with an increased number of stillbirths.¹¹¹ Phocomelia has been described with first trimester exposure to lindane in human pregnancy.¹¹² The itch of scabies may persist for some time after elimination. Application of **calamine** lotion and a sedative **antihistamine** at night may be needed. (See NMIC bulletin 1996; Vol 2: No 4)

THREADWORMS

Threadworm (pinworm) infection is commonly encountered in pregnancy, particularly in women who have other young children.¹¹³ **Anthelmintics** are contra-indicated in the first trimester.^{17,48,113-4} The mainstay of treatment is a rigid regimen of **personal hygiene**. Vigorous scrubbing of hands and nails after each bowel movement, avoiding scratching the anal area and daily bathing, with particular attention to the perianal area, is

recommended.^{17,48,60,113-4} Fingernails should be trimmed regularly.¹¹³ Threadworms produce large numbers of eggs and clothing and bed-linen rapidly become infested. Daily washing of clothing and linen is recommended. Pyjamas should be worn in preference to a nightdress.¹¹⁴ Strict adherence to these measures should break the reinfection cycle and the infestation should clear up within 3-6 weeks.^{17,114} At the same time, all other family members should receive appropriate drug treatment, even if asymptomatic.¹¹³⁻⁴

If treatment is required it should be deferred until after the first trimester; piperazine is the first-line agent used.¹¹³⁻⁴ There have been 2 case reports of fetal abnormalities associated with **piperazine** exposure.¹¹⁴ **Mebendazole**, **thiabendazole** and **albendazole** have been found to have embryotoxic and teratogenic in animals and are not recommended in early pregnancy.³⁵ Where perianal itching causes insomnia in early pregnancy, a **cream** containing a **local anaesthetic** or **soothing agent** may be beneficial.

URINARY TRACT INFECTIONS

Bacteruria is a common condition in pregnancy and is associated with significant maternal and neonatal morbidity.¹¹⁵⁻¹¹⁹ Approximately, 10% of pregnant women will have asymptomatic bacteriuria (ASB); if untreated, 40% of these will develop a symptomatic UTI.^{17,18,51} *E. coli* is the organism implicated in the majority of cases.¹¹⁶⁻⁸ The infection may present in the lower (**cystitis**) or upper (**acute pyelonephritis**) urinary tract. Acute pyelonephritis is one of the most common reasons for hospital admission in pregnancy.^{17,120} Fetal risks associated with a UTI include abortion, preterm labour, LBW, fetal infection and perinatal death. Selective screening of pregnant women for ASB is recommended at the first antenatal visit.¹⁸ Risk factors for ASB include a previous history of UTI, diabetes mellitus and renal disease.¹⁷ Those with a positive result should be treated with a 7 day course of antibiotics, even if asymptomatic and followed-up.

The choice of antibiotic should depend on MSU culture sensitivities.^{17,116-118,120} **Amoxycillin**, **nitrofurantoin** and **cephalexin** may be used first-line. Nitrofurantoin frequently causes nausea which may compromise compliance. Single doses of amoxycillin (3g) or cephalexin (2g), depending on sensitivity, have proved effective for UTI. Generally however a 1 week treatment course is recommended.¹²⁰ Quinolones, tetracyclines and co-amoxiclav are not recommended. Use of trimethoprim should be restricted to the second and third trimesters. If urine culture remains positive after 7 days of treatment, specialist advice should be sought. Prophylaxis with nitrofurantoin (50mg at night) is indicated where three or more recurrent episodes of UTI have occurred. Approximately 15% of women will have a recurrence, and so regular checks for ASB, at 4-6 weekly intervals, is recommended.

VENOUS THROMBOSIS

A patient who is maintained on oral anticoagulants for prevention of thrombosis should be advised against getting pregnant. Warfarin is highly teratogenic.¹²¹⁻⁸ Malformations associated with warfarin exposure in utero include chondrodysplasias, stippled epiphysis and optic atrophy.¹²¹⁻⁸ The period of risk is between 6 and 12 weeks gestation.¹²³ Fetal exposure to warfarin in the second and third trimesters has been associated with growth and mental retardation, blindness and fatal intraventricular haemorrhage.¹²³ If a patient conceives on warfarin the drug should be discontinued immediately. If anticoagulation is necessary, heparin is the drug of choice.

COMMON QUESTIONS PATIENTS ASK IN PREGNANCY.

Q 1. Is a multivitamin and mineral preparation recommended during pregnancy?

Vitamin and mineral supplementation during pregnancy should not be necessary providing the mother is eating a well-balanced diet and is not suffering from a malabsorption syndrome. The only supplements considered essential are **folic acid**, to prevent neural tube defects (NTDs) and **iron** to prevent anaemia. Folic acid is given in the first trimester. In women with a family history of NTDs, or those on a sub-optimal diet, folic acid supplementation prior to conception is recommended. Iron supplementation should be reserved for the second and third trimesters. Iron should not be given in early pregnancy as it aggravates nausea and vomiting and so reduces compliance. A daily dose of 60 mg elemental iron, after food, should suffice. Doses greater than 115 mg

elemental iron can cause nausea and vomiting. Generic iron preparations are preferable as these are much cheaper. Many women self-medicate with OTC multivitamins. Caution is advised as Vitamin A is neurotoxic to the foetus and unnecessary supplementation is contra-indicated.¹²⁹⁻³² High dose Vitamin A has been associated with craniofacial, CNS, cardiac and thymic malformations.¹²⁹ The maximum RDA of vitamin A is 1200 IU and should not be exceeded. Pregnant women should also be advised to avoid eating liver as this is a particularly rich source of Vitamin A.¹³³

Q 2. *Are herbal preparations safe to take in pregnancy?*

Many women take herbal preparations (e.g. teas) during pregnancy and these are often recommended in health food shops. However, even less information is available on the safety of herbal medicines than for orthodox medicines. Chinese herbal preparations may be particularly toxic.¹³⁴ Many are adulterated with undeclared drugs and lead, arsenic and mercurial compounds.¹³⁵ Several are used therapeutically (e.g. "yellow daphne", "mussaenda") to terminate early pregnancy.¹³⁶⁻³⁷ Others have been associated with a high incidence of neonatal jaundice.¹³⁸ Herb-induced hepatitis has been described in pregnancy.¹³⁹ Maternal fatality has been described within 30 minutes of drinking a Chinese herbal tea.¹⁴⁰ "Herbal health tonics" are also freely available. These should be avoided, especially in early pregnancy, as they have a high alcohol content (up to 14%). Fetal alcohol syndrome has been attributed to maternal ingestion of health tonics.¹⁴¹ Traditionally, some natural preparations have been used effectively in pregnancy (eg. rhubarb for hypertension, raspberry leaves for uterine tone), although safety data is limited.¹⁴²⁻³ Physicians and pharmacists should stress to women of child-bearing age the importance of avoiding "natural" herbal remedies.

Q 3. *Are hair products e.g. dyes, perming solutions safe to use in pregnancy?*

Animal studies have failed to show that exposures to hair care products have any harmful effects on the developing fetus. Many of the currently available products have not however been tested on animals.⁴⁷ Generally it is thought that such preparations are of no risk to the fetus. It would be advisable to use agents such as perming lotions in a well-ventilated area.

Q 4. *Are video-display units (VDU's) potentially harmful to the foetus?*



Many expectant mothers are concerned about the potential danger of VDU emissions on the developing foetus.¹⁴⁴ There have been a number of anecdotal reports of miscarriage in VDU operators, however larger epidemiological studies have failed to confirm any such link ^{47,145} Similarly, no increase in malformations has been observed in infants born to VDU operators..

Q 5. *Is malaria prophylaxis safe in pregnancy?*

Resistance to malaria decreases during pregnancy and, if infected, the disease is more severe in the pregnant population.¹⁴⁶⁻⁷ Ideally, travel to such areas should be avoided during the first trimester. If the journey is unavoidable, chloroquine and proguanil are safe and should be given, at the risk of chloroquine resistance.¹⁴⁶⁻⁷ Folic acid supplementation is essential in the first trimester as proguanil is a folate antagonist ¹⁴⁷. Mefloquine is highly teratogenic and should not be taken in the first trimester; it may be taken safely in the second and third trimesters.¹⁴⁸⁻⁹ Sexually active women of child-bearing age should use contraception while taking mefloquine and for 3 months subsequently.

Q 6. *Are travel vaccinations safe in pregnancy?*

Live vaccines (e.g. polio, yellow fever) should not be routinely administered to pregnant women and ideally should not be administered during the first four months of pregnancy.¹⁵⁰ Live vaccines are not teratogenic or embryotoxic.¹⁵⁰ However, they may cause febrile reactions which have been associated with spontaneous abortions.¹⁵⁰⁻¹ Where vaccination is indicated, prophylactic paracetamol should be given. Inactivated vaccines are generally safe except for those which cause febrile reactions.¹⁵² Typhoid, in particular, is associated with fever.¹⁵² If a pregnant women decides to travel to an area where these diseases are endemic it is essential that she is fully immunised.

Q 7. *Is air travel safe in pregnancy?*



Air travel is not recommended after 36 weeks of pregnancy.¹⁵³ Where there is a history of multiple pregnancy, preterm delivery or bleeding, flying should be avoided throughout the third trimester.¹⁵³ Reduced cabin pressures at higher altitudes may cause hypoxia. Long-haul flights may precipitate venous thromboembolism.¹⁵⁴⁻⁶ Pregnant women should be advised to walk around the cabin at regular intervals during long flights.

Q 8. *Is acupuncture of benefit in pregnancy?*

Controlled studies on the use of acupuncture in pregnancy are limited. However, stimulation of the PC6 acupuncture point has been reported to have an anti-emetic effect.¹⁵⁷⁻⁸ This has been used effectively in the prevention of anaesthesia-induced nausea and vomiting by midwives trained in acupuncture at caesarean section.¹⁵⁹⁻⁶⁰ Acupressure wristbands have proved effective in alleviating morning sickness.¹⁶¹⁻² These bands are available from pharmacies and offer a non-drug approach to the management of nausea and vomiting. They tend to be more effective if used early in the symptom experience.¹⁶² In non-pregnant patients acupuncture has been reported to be as effective as metoprolol in migraine prophylaxis.¹⁶³



The NMIC answers enquires from health care professionals only



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