






TREATMENT OF COMMON MEDICAL PROBLEMS IN PREGNANCY PART I

-  The use of prescription and over-the-counter (OTC) medicines should be avoided during pregnancy, unless considered essential.
-  Drugs should be prescribed only if the expected benefit to the mother outweighs the potential risk to the foetus, and mothers should be made aware of such risks..
-  The first trimester is the period of greatest teratogenic risk. Drug use in all women of child-bearing potential should reviewed as 50 % of pregnancies are "unplanned".
-  New drugs should be avoided. Older, more established preparations are preferable during pregnancy.
-  For self-limiting illnesses, reassurance and lifestyle changes may suffice

INTRODUCTION

Enquiries on the use of drugs in pregnancy are amongst the most commonly received by the Centre. As the majority of medicines are not licensed for use in pregnancy, definitive advice cannot be offered. The final decision to use a medicine will rest with the prescriber, following risk benefit analysis and discussion with the patient. The aim of these two bulletins is to provide the prescriber with relevant information to assist in the treatment of common medical conditions in pregnancy.

Since the thalidomide disaster there has been significant concern over the safety of drugs in pregnancy. Approximately, 1-3 % of birth defects are due to in utero drug exposure.^{1,2} The classic teratogenic period is week 3-8 post-conception, when the major organ systems are formed (organogenesis).^{3,4} Teratogenic effects are probably dose related.⁵ Prior to week 3, exposure to a drug has an "all-or-nothing" effect on the embryo (i.e. survival or death) and from week 9 onwards, may affect growth and functional development of the foetus.^{3,4,6,7} Almost all drugs, except those of high molecular weight, cross the placenta and have the potential to cause foetal harm.^{6,8} Prescribers can reduce this risk by using medicines considered safe in pregnancy. This also applies to non-pregnant women of child bearing-age, as almost 50 % of pregnancies are unplanned.⁷

Pregnant women are predisposed to a number of common ailments which may require treatment for control of symptoms. In addition, there may be a pre-existing health problem requiring continued therapy. The challenge is to choose a treatment that is both effective for the mother and harmless to the foetus; this may not be the preferred treatment in the non-pregnant population.⁸

ASTHMA

Asthma is one of the most common chronic illnesses in pregnancy with a prevalence of 3-5%.⁹ Many asthmatics present with worsening of their symptoms because they have stopped or reduced their usual medication due to fear of it harming their baby.^{9,10} Patients should be reassured that uncontrolled asthma poses a much greater risk to both mother and foetus than the medications used to treat it. Asthma medications have a good safety profile in pregnancy.^{11,12,13} Poorly controlled asthma is associated with higher rates of miscarriage, preterm delivery, low birthweight (LBW), intra-uterine growth reduction (IUGR), hypertension, pre-eclampsia and perinatal mortality.^{13,14} However, with careful monitoring and appropriate treatment, most patients will remain stable.⁹⁻¹⁷

Management of asthma is essentially the same as in the non-pregnant population. Avoidance of trigger factors is particularly important in pregnancy.¹⁶ Inhaled medications are preferable to systemic treatment. Terbutaline or salbutamol should be used first-line; if required on a regular basis (>once daily), a steroid inhaler should be prescribed.¹⁸ **Beclomethasone** is the inhaled steroid of choice.¹³ There is insufficient data

to recommend the use of **salmeterol** in pregnancy, although no adverse effects have been reported.¹⁸ Safety data on the use of antimuscarinics eg; **ipratropium**, are limited, although no adverse effects have been reported.¹⁷ **Sodium cromoglycate** may be useful prophylaxis for individuals with an allergic component.¹⁴ **Aminophylline** (up to 10mg/kg/day) should be reserved for women whose disease is not adequately controlled with inhaled steroids and beta-agonists.¹⁸ Monitoring of serum theophylline levels is recommended.¹² Aminophylline is considered safe in pregnancy, although third trimester use has been associated with neonatal irritability and apnoea.^{3,19} Short courses of oral **prednisolone** are safe for acute exacerbations and should not be withheld when clearly indicated.^{13,18,19} Prolonged use of oral steroids has been associated with gestational diabetes and foetal and neonatal adrenal insufficiency.¹⁴ Asthmatic patients should be reviewed every 4-6 weeks during pregnancy.¹¹

BACTERIAL VAGINOSIS

Bacterial vaginosis (BV) is the most prevalent form of vaginitis and is due to an overgrowth of anaerobic bacteria.²⁰⁻²² It is characterised by profuse malodorous discharge, although up to 50% of women are asymptomatic.²¹⁻²³ BV is not benign; associated risks include preterm delivery, premature rupture of membranes (PROM), chorioamnionitis, post-partum endometritis, pelvic inflammatory disease and abnormal uterine bleeding.²²⁻²⁵ Testing for BV is currently recommended where there is symptomatic vaginal discharge or an obstetric history of preterm labour, BV or PROM.²¹⁻²⁸

The antibiotics effective in treating BV are **metronidazole** and **clindamycin**.²³ Both appear safe, even in the first trimester.²¹⁻²² Oral metronidazole (400mg tds for 7 days) or intravaginal 2% clindamycin cream (5mg daily for 7 days) is recommended.²³ Gastrointestinal upset and irritation can be a problem with metronidazole. Single dose oral metronidazole (2g) is an alternative in non-compliant patients (but less effective). Metronidazole suppositories are often used effectively as pessaries (500mg bd for 7 days) to minimise systemic effects, although not a licensed indication. There is no rationale for combined oral and vaginal administration. Oral clindamycin, although effective, is not recommended because of the potential for maternal skin reactions and pseudomembranous colitis. Clindamycin cream is associated with a higher incidence of candidal infection.²⁹ Amoxycillin and erythromycin are ineffective against BV.²³⁻²⁶ Douching is not recommended as it may cause upper genital infection.²⁹

CANDIDIASIS

Vulvovaginal candidiasis (VVC) is 10-20 times more common in pregnancy.^{18,30,31} Treatment is necessary to provide symptomatic relief and prevent foetal candida sepsis.^{32,33} Topical imidazoles (e.g. **clotrimazole**, **miconazole**) are the treatment of choice, either as pessaries or cream inserted high into the vagina. **Nystatin** pessaries are equally effective. Oral antifungal agents should be avoided in pregnancy.^{17,31,33,34} Craniofacial, skeletal and cardiac defects have been reported in infants exposed to long term **fluconazole** in utero.^{33,35} The relapse rate for VVC is higher in the pregnant population.³⁰ Recurrence may also occur if a full treatment course is not completed. Reinfection may be due to the partner and they should be treated accordingly.

CHLAMYDIAL INFECTION

Chlamydia trachomatis is the most common sexually transmitted disease in Europe.^{36,37} Prevalence of chlamydial infection in pregnancy varies widely and is influenced by age and socioeconomic status; estimates range from 2-37%.³⁸ Pregnancy may render the cervix more prone to infection.³⁹ Symptoms include non-specific urethritis, salpingitis and mucopurulent cervicitis, although the condition is often asymptomatic.^{36,40} Chlamydial infection is associated with preterm delivery, LBW and PROM and post-partum endometritis-salpingitis.^{36,37,41} Approximately 60-70% of infants born to infected mothers will acquire the infection during delivery.³⁹ Manifestations include neonatal conjunctivitis, blepharitis and chlamydial pneumonia; 15-20% of infants will carry the infection for up to 18 months.³⁹

Erythromycin (500mg qds for 7 days) is the treatment of choice in pregnancy.^{36,40} Many women are intolerant of its gastrointestinal effects (especially nausea).³⁷ **Amoxycillin** (500mg tds for 7 days) is a reasonable alternative.^{37-40,42-44} Recently, a single dose of **azithromycin** (1g) has proved effective with no known adverse foetal effects.^{45,46} Azithromycin may be particularly useful where poor compliance is a

problem. Both tetracycline and quinolones are contra-indicated in pregnancy due to adverse effects on developing bones and teeth.⁴⁰

COLDS AND COUGHS

Cough and cold medications are among the most commonly used drugs in pregnancy.^{47,48} Pregnant women are at particular risk when they have other young children.⁴⁹ OTC preparations contain a range of drugs including **antihistamines** in combination with an **analgesic** and **antitussive** or **expectorant**. Many formulations contain a **decongestant**. Most **antihistamines** are considered safe in pregnancy for short-term use.^{50,51} **Paracetamol** is the analgesic of choice. Opioid cough suppressants are not recommended.⁶ Expectorants such as **guaiphenesin** are safe but usually ineffective.⁶ **Pseudoephedrine** is the decongestant of choice but should be avoided in hypertensive patients.^{47,51} Simple remedies should be recommended rather than "cure all" preparations.^{6,52} Topical agents should be recommended in preference to systemic treatments, especially in early pregnancy. Simple lozenges, gargles, nasal sprays and chest rubs are considered safe to take at any stage.^{51,52} Preparations containing alcohol, NSAIDs and iodine should be avoided.⁴⁹ Iodine may affect foetal thyroid function and NSAIDs can affect developing renal and cardiac function.^{47,49}

CONSTIPATION

Approximately 40% of women experience constipation, especially in the third trimester.⁵³ Causative factors include hormone-related changes in gastrointestinal motility and fluid absorption, pressure of the uterus on the bowel, lack of exercise and certain medications (e.g. iron supplements).^{6,20,53} Patients should be advised to eat a high fibre diet (cereals, fresh fruit, vegetables), drink plenty of water and take regular exercise. Laxatives should only be prescribed when these measures have failed.

When treatment is required, bulking agents (e.g. **bran**, **ispaghula**, **sterculia**, **methylcellulose**) should be used first-line.^{6,20,53,54} **Lactulose** (30ml daily) is also widely prescribed but is more expensive. Fibre laxatives and lactulose are not systemically absorbed and are therefore safe to use. Patients should be advised that it may take several days before they have an effect. They must be taken regularly to prevent constipation. Lactulose is contra-indicated in lactose intolerance and galactosemia.¹⁸ Lactulose is safe to use in diabetics.

Stimulant laxatives (e.g. **bisacodyl**, **phenolphthalein**) may be uterotonic and are therefore best avoided.^{6,20,51} **Senna** is considered safe to use for short-term use and under medical supervision.⁶ Senna may colour the urine. Other anthroquinones, **aloe** and **danthron**, have been associated with congenital malformations.^{18,53} Liquid paraffin and lubricants (e.g. **castor oil**) are contraindicated; these may cause malabsorption of fat soluble vitamins resulting in neonatal coagulation defects.^{18,53} **Saline cathartics** (e.g. **magnesium hydroxide**) may cause electrolyte depletion and fluid loss and are not recommended.^{50,53} The safety of **docusate sodium** in pregnancy has not been established.⁶

HAEMORRHOIDS

Haemorrhoids are very common in pregnancy.^{6,54} Women prone to haemorrhoids often present for the first time during pregnancy. They are more common in multiparous women and are exacerbated by constipation and straining during labour. Possible aetiological factors include high pressure in the pelvic veins and hormonal effects on the haemorrhoidal plexus.¹⁸ Symptoms include rectal bleeding, pruritis and perineal pain. Treatment is often not needed. Otherwise, a soothing antiseptic cream with a mild astringent may provide local relief. If swollen and painful, bed rest and application of a cold compress is recommended.⁶ Topical steroids may be beneficial. Haemorrhoidectomy may be required in severe cases.¹⁸

HAYFEVER

Pregnant women commonly present with allergic rhinitis (hayfever).⁵⁵ Avoidance of trigger factors may suffice in some patients.¹⁷ Topical agents should be used in preference to systemic antihistamines.⁵⁶

Topical corticosteroids may also be used but high doses of **systemic corticosteroids** should be avoided.⁵⁶ **Sodium cromoglycate** is also safe.⁵⁶ **Intranasal decongestants** may be of benefit and are safe to use, but should not be given to hypertensive patients.⁴⁹ Where local treatments are ineffective, a systemic antihistamine may be given. **Chlorpheniramine** and **promethazine** are the agents of choice.⁵⁶ (*See NMIC bulletin 1997; Vol 3:No 2.*)

HEARTBURN

Patients should be reassured that heartburn is normal in pregnancy; it affects up to 80% of pregnant women.^{8,18} Lifestyle modifications and dietary advice are sufficient to alleviate symptoms in over half of patients.^{18,57} Patients should be advised to avoid reflux-provoking positions, to stop smoking and to cut out foods which are known to aggravate the condition.^{8,18,53,58,59} Patients should eat small regular meals, rich in carbohydrate, and should not eat or drink liquids, except water, for 3 hours before retiring.^{53,58}

If symptoms persist without relief, **antacids** may be prescribed, even in the first trimester. Approximately, one-third of women take antacids during pregnancy.¹⁸ Preparations include **aluminium**, **magnesium** and **calcium** salts and non-absorbable **alginates**. Compound preparations are no more efficacious than simple mixtures and are more expensive.^{17,60} Aluminium mixtures may exacerbate constipation; magnesium salts may be useful for patients prone to constipation. Most obstetricians prefer calcium mixtures.⁸ Long-term use of **magnesium trisilicate** should be avoided.¹⁸ **Sodium bicarbonate** should also be avoided as it may precipitate metabolic alkalis and fluid overload in the foetus and mother.⁵⁷ Alka-seltzer tablets should not be recommended as they contain **aspirin**.⁵⁴ Preparations containing **local anaesthetics**, **antispasmodics** and **gastric motility agents** should be avoided in the first trimester.⁶⁰ H₂-receptor antagonists such as **cimetidine** and **ranitidine** and **proton pump inhibitors** are not recommended for management of heartburn in pregnancy.^{58,61} Dyspepsia related to peptic ulceration is unusual in pregnancy.²⁰

INFLAMMATORY BOWEL DISEASE

Active inflammatory bowel disease (IBD) is associated with higher rates of miscarriage, more complicated pregnancies and LBW infants.⁶² Women with IBD should be encouraged to become pregnant when their disease is quiescent.¹⁸ Relapse is common during pregnancy, especially in the first trimester.¹⁸ Prenatal supplementation of **folate**, **vitamin B12** and **vitamin E** is advised.^{8,60} **Vitamin D** deficiency is common in Crohn's disease.¹⁸ **Iron** supplementation may be needed in chronic blood loss. Patients should be advised to drink plenty of fluids and eat a high fibre diet (if strictures are excluded).¹⁸ A hydrophilic laxative, such as **lactulose**, may be beneficial.¹⁸

Maintenance drug treatment for IBD during pregnancy is similar to that for non-pregnant patients.^{8,17,18,63} **Sulphasalazine** is safe to use throughout gestation.^{8,17,18,20,62-7} Sulphasalazine impairs absorption of folate and so daily supplementation with **folic acid** (5mg daily) is essential.^{17,18,20} Experience with **mesalazine** and **olsalazine** is limited, however, no foetal abnormalities have been reported to date.^{8,62,66,68} These agents offer a reasonable alternative in patients intolerant of side effects related to the sulphapyridine moiety of sulphasalazine.^{62,66} Patients maintained on mesalazine or olsalazine prior to pregnancy may continue on the same medication.¹⁷

The use of **antidiarrhoeals** and **antimotility agents** is not recommended. Many contain **anticholinergics** which have been associated with foetal bradycardia and congenital abnormalities.¹⁸ Moreover, diarrhoea is an indicator of disease activity. **Topical corticosteroids** (rectal foams, suppositories, enemas) are useful for control of acute exacerbations while minimising systemic exposure. Oral corticosteroids should be used, if indicated, at the lowest effective dose. In severe cases, hospital admission for bed rest and aggressive therapy is necessary. **Immunosuppressants** are not recommended as they can cause infertility in the female foetus and chromosomal abnormalities.^{18,63,65} **Azathioprine**, has been used in resistant cases of IBD.¹⁷

INSOMNIA

Insomnia is a common feature of pregnancy. Management should focus on psychology rather than pharmacology.⁶⁹ Good **sleep hygiene** and **relaxation techniques** should be recommended. Other physical

symptoms which disturb sleep (e.g.pain) should be treated in their own right.⁷⁰ The use of hypnotics should be avoided if possible.^{3,71,72} **Benzodiazepines** (BZDs), especially **diazepam**, are among the most widely prescribed drugs during pregnancy.⁷³

First trimester exposure to BDZs has been associated with increased risk of facial clefts (lip/palate), cardiac malformations, growth retardation and CNS defects.^{71,73} However recent analyses have failed to confirm these associations.^{73,74} Late third trimester exposure is a greater concern. Accumulation of BDZs in utero can result in "floppy infant syndrome" or neonatal withdrawal effects.^{69,71,73} If a BDZ is considered essential, a short-acting agent such as **temazepam** is preferable. The lowest effective dose should be given for the shortest possible time, and discontinued well prior to delivery.⁷³ **Chloral hydrate** has been widely prescribed in pregnancy, but safety data is lacking.⁷¹ The newer agents **zopiclone** and **zolpidem** should be avoided.^{71,75}

See Part II for References.