Prescribing medicines in pregnancy

4th edition

An Australian categorisation of risk of drug use in pregnancy

TGA THERAPEUTIC GOODS ADMINISTRATION

Australian Drug Evaluation Committee

The Australian categorisation consists of the following categories:

Category A
Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.

Category C
Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details.

Category B1
Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

Studies in animals have not shown evidence of an increased occurrence of fetal damage.

Category B2
Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.

Category B3
Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is considered uncertain in humans.

Category D
Drugs which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects. Accompanying texts should be consulted for further details.

Category X
Drugs which have such a high risk of causing permanent damage to the fetus that they should not be used in pregnancy or when there is a possibility of pregnancy.

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From the Chairman

It is now ten years and four editions since *Medicines in Pregnancy* was first produced by the Australian Drug Evaluation Committee to assist health professionals in the appropriate prescription of drugs in pregnancy. Over one hundred new medicines have been evaluated and approved for registration in Australia since the publication of the last edition in 1996 and have been added to the current booklet. In addition, the introduction of colour printing has allowed a revision of the layout of the text to improve the clarity of information provided.

This edition has been retitled *Prescribing Medicines in Pregnancy*, to emphasise the purpose of the booklet — guiding the prescriber in the correct choice of medication when drug therapy is required in pregnancy. This booklet is not intended for use in the more complex situation of inadvertent drug exposure in early pregnancy, and for this circumstance, the reader is referred to the Obstetric Drug Information Services listed in Appendix B.

The Australian Drug Evaluation Committee is keen to ensure that appropriate therapeutic options are available to all women needing medical treatment or preventative therapy during pregnancy, with minimisation of any associated risk to the fetus. An essential prerequisite, and the aim of this booklet, is the provision of accurate, concise information as a basis for informed consent and rational decision making. As always, the Committee welcomes feedback and is most grateful to those who have offered constructive suggestions about past editions.

Dr Rosemary Ayton
Chairman
Medicines in Pregnancy Working Party

CONTENTS

CONTENTS

INTRODUCTION

One in twenty five (1:25) babies born in this country has a birth defect. A small proportion of these birth defects are caused by medications taken by the mother during pregnancy.

This categorisation is intended to provide information which can be used by health professionals as the basis for rational decision making when **planning** the medical management of pregnant patients or those intending to become pregnant. **Therefore, in many cases, this categorisation will not be appropriate as the sole basis of decision making after inadvertent or accidental drug exposure has occurred during pregnancy.** In this context, there can be no substitute for expert information based on a rigorous appraisal of all the specific circumstances in each case. Appendix B should be used to ensure that appropriate advice is obtained in such situations. **This categorisation applies only to recommended therapeutic doses in women in the reproductive age group. In situations such as overdose, occupational exposure and others when the recommended therapeutic dose is exceeded, it cannot be assumed that the classifications assigned to individual medicines are valid.**

Most medicines cross the placenta. This categorisation has taken into account the known harmful effects of medicines on the developing baby, including the potential to cause birth defects, the potential to cause unwanted pharmacological effects around the time of birth (effects which may or may not be reversible), and the potential to cause problems such as cancer in later life. However, it does not take into account the rare circumstance of an idiosyncratic reaction in the neonate to a medicine which crosses the placenta.

All gestational ages referred to in this booklet are based on the time of conception. A medicine may have more than one harmful effect on the

developing baby depending on the timing of exposure. During the first two weeks of development, from conception to the first missed period, the embryo is thought to be resistant to any teratogenic effects of medicines. The critical period of embryonic development, when the organ systems develop, starts at about 17 days post-conception and is complete by 60-70 days. Exposure to certain medicines during this period (17-70 days) can cause major birth defects. In general, exposure to medicines beyond 70 days post-conception is not associated with the induction of major birth defects.

However, some medicines can interfere with functional development of organ systems in the second and third trimesters and produce serious consequences. An important example is renal dysfunction in the fetus caused by ACE inhibitors taken during the second and third trimesters.

Also, the developing central nervous system, because of its prolonged period of histogenesis and functional maturation, can be damaged by exposure to certain medicines in the second and third trimesters, resulting in problems such as mental retardation, cerebral palsy or deafness.

In addition to gestational timing, the actual dose being given, compared to a known harmful dose, needs to be considered in assessing whether there are likely to be any adverse effects.

The list of categorised medicines includes most of those used commonly in Australia. The categorisation is based on currently available evidence and changes may be necessary from year to year as new evidence is presented and analysed. The class statements in italicised blue font should be considered integral information about all of the drugs covered in that class.

INTRODUCTION

For pharmaceutical products containing two or more active medicines, the categorisation of the combination is based on the component for which the categorisation is most restrictive. When a medicine is only to be used in men, it will not be found in the booklet although it will have a pregnancy category in the Product Information.

The Australian categorisation consists of the following categories:

Category A
Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.

Category C
Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details.

Category B1
Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

Studies in animals have not shown evidence of an increased occurrence of fetal damage.

Category B2

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.

Category B3

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is considered uncertain in humans.

Category D

Drugs which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects. Accompanying texts should be consulted for further details.

Category X

Drugs which have such a high risk of causing permanent damage to the fetus that they should not be used in pregnancy or when there is a possibility of pregnancy.

Note: For drugs in the B1, B2 and B3 categories, human data are lacking or inadequate and subcategorisation is therefore based on available animal data. **The allocation of a B category does NOT imply greater safety than the C category**. Drugs in category D are not absolutely contraindicated in pregnancy (e.g. anticonvulsants). Moreover, in some cases the 'D' category has been assigned on the basis of 'suspicion'.

Due to legal considerations in this country, sponsor companies have, in some cases, applied a more restrictive category than can be justified on the basis of the available data.

In some cases there may be discrepancies between the published Product Information and the information in this booklet due to the process of ongoing document revision.

Australian categorisation of drugs

(grouped by therapeutic class)

ALIMENTARY SYSTEM

HYPERACIDITY, REFLUX, ULCERS

Alginates/antacids — A

Bismuth subcitrate — B2

Cimetidine, cisapride, famotidine, ranitidine, sucralfate — B1

Lansoprazole, nizatidine, omeprazole, pantoprazole — B3

Misoprostol — X

This drug can produce serious birth defects. It also can cause miscarriage that could lead to potentially dangerous bleeding.

ANTISPASMODICS

Atropine — A

Glycopyrrolate, hyoscine-N-butylbromide, mebeverine, propantheline — B2

LAXATIVES

Bisacodyl, cascara, docusate sodium, senna — A

Dicyclomine hydrochloride — B1

Phenolphthalein — B2

ANTIDIARRHOEALS

Diphenoxylate — C

This drug is chemically related to the narcotic analgesic pethidine. Narcotic analgesics may cause respiratory depression in the newborn infant. This drug should not be given at or near term.

Hyoscyamine — B2

Loperamide — B3

Mesalazine, olsalazine — **C**

Non-steroidal anti-inflammatory drugs inhibit prostaglandin synthesis and, when given during the latter part of pregnancy, may cause closure of the fetal ductus arteriosus, fetal renal impairment, inhibition of platelet aggregation, and delay labour and birth. Continuous treatment with non-steroidal anti-inflammatory drugs during the last trimester of pregnancy should only be given on sound indications. During the last few days before expected birth, agents with an inhibitory effect on prostaglandin synthesis should be avoided.

Sulfasalazine — **A**

Systemic budesonide — **B3**

CHOLELITHOLYTICS

Chenodeoxycholic acid — **B3**

CARDIOVASCULAR SYSTEM

ANTIHYPERTENSIVES

Clonidine, doxazosin — **B3**

Diazoxide — **C**

This drug may cause fetal bradycardia. Hyperglycaemia has been observed in the newborn. Diazoxide is a potent relaxant of uterine smooth muscle and may inhibit uterine contraction if given during labour. Diazoxide should be used with extreme caution during pregnancy.

Guanethidine, methyldopa — **A**

Hydralazine — **C**

Following intravenous administration, hydralazine has been associated with fetal distress and fetal arrhythmia in the last trimester of pregnancy.

Minoxidil — **C**

This drug has been associated with hypertrichosis in the newborn infant following exposure in utero.

Prazosin, terazosin — **B2**

Sodium nitroprusside — **C**

Short term use for the control of hypertensive crises may be safe provided that the pH and cyanide concentrations in maternal blood are monitored.

ANGIOTENSIN CONVERTING ENZYME (ACE) INHIBITORS

When taken during the second and third trimesters, ACE inhibitors cause a range of abnormalities including renal dysfunction and oligohydramnios. These can be associated with fetal death in utero.

Although no adverse fetal effects have been linked to first trimester drug use of ACE inhibitors, the number of exposures

reported is too small to determine conclusively that ACE inhibitors are safe in the first trimester. Pregnant women who are taking ACE inhibitors should be changed as quickly as possible to other antihypertensive medication to maintain normal blood pressure. It is generally advisable not to use ACE inhibitors for the management of hypertension in women who are likely to become pregnant.

Captopril, cilazapril, enalapril, fosinopril, lisinopril, perindopril, quinapril, ramipril, trandolapril **D**

ANGIOTENSIN II RECEPTOR ANTAGONISTS (ARAS)

When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death in the developing fetus.

Although no adverse fetal effects have been linked to first trimester drug use of ARAs, the number of exposures reported is too small to determine conclusively that ARAs are safe in the first trimester. Pregnant women who are taking ARAs should be changed as quickly as possible to other antihypertensive medication to maintain normal blood pressure. It is generally advisable not to use ARAs for the management of hypertension in women who are likely to become pregnant.

Candesartan cilexetil, eprosartan, irbesartan, losartan, valsartan **D**

CALCIUM CHANNEL BLOCKERS

These drugs carry the potential to produce fetal hypoxia associated with maternal hypotension.

Amlodipine, diltiazem, felodipine, isradipine, nicardipine, nifedipine, nimodipine, nisoldipine, verapamil **C**

CARDIOVASCULAR SYSTEM

BETA-ADRENERGIC BLOCKING AGENTS

These agents may cause pharmacological effects such as bradycardia in the fetus and newborn infant.

Alprenolol, atenolol, betaxolol, bevantolol, carvedilol, esmolol, labetalol, levobunolol, metoprolol, oxprenolol, pindolol, propranolol, sotalol, timolol **C**

DIURETICS

Carbonic anhydrase inhibitor

Acetazolamide **B3**

Thiazides, related diuretics and loop diuretics

These drugs may cause electrolyte disturbances in the fetus. Neonatal thrombocytopenia has been reported with thiazides and related diuretics. Loop diuretics, like frusemide and bumetanide, are probably also associated with this risk. During the latter part of pregnancy products of this type should only be given on sound indications, and then in the lowest effective dose.

Bendrofluazide, bumetanide, chlorothiazide, chlorthalidone, clopamide, cyclopenthiazide, ethacrynic acid, frusemide, hydrochlorothiazide, indapamide, mefruside, methychlothiazide, metolazone, quinethazone **C**

Potassium sparing diuretics

Amiloride, triamterene **C**

These drugs may result in electrolyte disturbances in the fetus.

Spironolactone **B3**

This drug carries the potential to cause feminisation of the male fetus and should be avoided during pregnancy.

ANTIARRHYTHMICS

Adenosine, disopyramide, procainamide — B2

Amiodarone — C

Because of the long half-life of amiodarone and its major metabolite, and the potential to cause abnormal thyroid function and bradycardia in the fetus, its use is probably best avoided in the three months before and throughout the duration of pregnancy. When exposure of the fetus is unavoidable, thyroid function (including TSH) should be assessed promptly in the newborn infant.

Bretylium tosylate — C

This drug carries the potential for fetal hypoxia associated with maternal hypotension.

Flecainide — B3

Lignocaine — A

Mexiletine — B1

Quinidine — C

This drug is structurally similar to quinine, which in high doses, has been shown to cause fetal damage. It has been used to treat fetal cardiac arrhythmia

ANTIANGINA AGENTS

Glyceryl trinitrate, isosorbide mononitrate, perhexilene — B2

Isosorbide dinitrate, tirofiban hydrochloride — B1

Nicorandil — B3

CARDIOVASCULAR SYSTEM

HYPOLIPIDAEMIC AGENTS

The physiological hyperlipidaemia of pregnancy does not require treatment.

Atorvastatin, cerivastatin, fluvastatin, pravastatin, simvastatin — **C**

Cholesterol and other products of the cholesterol biosynthesis pathway are essential components for fetal development, including synthesis of steroids and cell membranes. Because of the ability of inhibitors of HMG-CoA reductase to decrease the synthesis of cholesterol and possibly other products of the cholesterol biosynthesis pathway, these drugs may cause fetal harm when administered to a pregnant woman.

Cholestyramine, colestipol, nicotinic acid — **B2**

Clofibrate, probucol — **B1**

Gemfibrozil — **B3**

CARDIAC INOTROPIC AGENTS

Digoxin and other cardiac glycosides — **A**

Milrinone — **B3**

ADRENERGIC STIMULANTS

Adrenaline, ephedrine, fenoterol, isoprenaline, orciprenaline, rimiterol, salbutamol, terbutaline — **A**

Dobutamine, phenylephrine, phenylpropanolamine, pseudoephedrine — **B2**

Dopamine — **B3**

Metaraminol — **C**

This drug may cause fetal hypoxia by constricting the uterine vessels thereby limiting placental perfusion.

VASODILATORS

Betahistine, glyceryl trinitrate, nicotinic acid B2

Dipyridamole, isosorbide dinitrate, nicotinyl alcohol, oxpentifylline, phentolamine, sildenafil citrate B1

Isoxsuprine C

Maternal isoxsuprine administration for prevention of premature labour has been associated with tachycardia, hypoglycaemia, hypocalcaemia, ileus and hypotension in the neonate.

Papaverine A

Phenoxybenzamine B2

This drug is known to be mutagenic and carcinogenic in rodents.

ANTIMIGRAINE PREPARATIONS

Dihydroergotamine, ergotamine, methysergide C

Standard oral dose regimens for migraine headaches in the first half of pregnancy do not appear to pose hazards to the fetus. Ergotamine induces uterine contraction and may therefore cause premature parturition or hypertonic labour. Larger doses or more frequent use may jeopardise the fetus because of the potential for impeding fetal blood supply.

Naratriptan, sumatriptan, zolmitriptan B3

Pizotifen B1

ANTICOAGULANTS AND THROMBOLYTIC AGENTS

All of these agents can produce placental haemorrhage and subsequent prematurity and fetal loss.

Abciximab C

Dalteparin, danaparoid, enoxaparin, nadroparin, C

CARDIOVASCULAR SYSTEM

Desirudin B3

Heparin C

Phenindione D

This drug can cause birth defects when used in the first trimester of pregnancy.

Ticlopidine B1

Warfarin D

Warfarin has been associated with the development of a specific embryopathy following exposure at 6 to 9 weeks post conception. Exposure following first trimester of pregnancy can cause fetal bleeding leading to CNS damage. There is also an increased risk of spontaneous abortion and perinatal bleeding. It should not be used in the last few weeks of pregnancy.

HAEMOSTATIC AGENTS

Aprotinin, eptacog alfa, tranexamic acid B1

Human coagulation factor IX C

The safe use of this drug during pregnancy has not been established in controlled clinical trials.

Kogenate, protamine B2

Aminocaproic acid, o rnipressin B3

FIBRINOLYTIC AGENTS

Alteplase, urokinase B1

Reteplase C

Streptokinase C

Only minimal amounts of streptokinase cross the placenta. Streptokinase-specific antibodies are found in fetal blood.

OTHER CARDIOVASCULAR AGENTS

DRUGS AFFECTING BLOOD AND HAEMOPOIETIC TISSUES

IRON AND HAEMOPOIETIC AGENTS

Erythropoietin, filgrastim, lenograstim, molgramostim	B3
Folic acid	A
Folinic acid	A
Oral iron preparations (with or without folic acid), parenteral iron preparations	A

ANALGESICS, ANTIPYRETICS

(See also non-steroidal anti-inflammatory drugs page 21)

OPIOID ANALGESICS

Opioid analgesics may cause respiratory depression in the newborn infant. Withdrawal symptoms in newborn infants have been reported with prolonged use of this class of drugs.

Alfentanil, buprenorphine, dextromoramide, dextropropoxyphene, fentanyl, hydromorphone, methadone, morphine, oxycodone, papaveretum, pentazocine, pethidine, phenoperidine, remifentanil, tramadol **C**

Aspirin **C**

Aspirin inhibits prostaglandin synthesis. When given late in pregnancy, it may cause premature closure of the fetal ductus arteriosus, delay labour and birth. Aspirin increases the bleeding time both in the newborn infant and in the mother because of its antiplatelet effects. Products containing aspirin should be avoided in the last trimester. Low-dose aspirin (100mg/day) does not affect bleeding time.

Codeine, dihydrocodeine **A**

Prolonged high-dose use of codeine prior to delivery may produce codeine withdrawal symptoms in the neonate.

Paracetamol **A**

HYPNOTICS AND SEDATIVES

Barbiturates

These drugs can give rise to hypotension, respiratory depression and hypothermia in the newborn infant. Continuous treatment during pregnancy and administration during labour should be avoided.

Amylobarbitone, pentobarbitone **C**

OTHER HYPNOTICS AND SEDATIVES

Chloral hydrate, chlormethiazole — **A**

Meprobamate — **C**

This drug may cause hypotension, respiratory depression and hypothermia in the newborn infant.

Zolpidem tartrate — **B3**

Zopiclone — **C**

This drug is likely to produce CNS depression in newborn infants when given during labour.

ANTIANXIETY AGENTS

Buspirone — **B1**

BENZODIAZEPINES

Benzodiazepines may cause hypotonia, respiratory depression and hypothermia in the newborn infant if used in high doses during labour. Withdrawal symptoms in newborn infants have been reported with prolonged use of this class of drugs.

Alprazolam, bromazepam, chlordiazepoxide, clobazam, clonazepam, clorazepate, diazepam, flunitrazepam, flurazepam, lorazepam, midazolam, nitrazepam, oxazepam, temazepam, triazolam — **C**

ANTIPSYCHOTIC AGENTS

Phenothiazines

When given in high doses during late pregnancy, phenothiazines have caused prolonged neurological disturbances in the newborn infant.

Chlorpromazine, fluphenazine, pericyazine, perphenazine, promazine, thiopropazate, thioridazine, trifluoperazine — **C**

Butyrophenones

When given in high doses during late pregnancy, butyrophenones may cause prolonged neurological disturbances in the newborn infant.

Droperidol, haloperidol C

OTHER ANTIPSYCHOTIC DRUGS

Clozapine C

The adverse pharmacological and toxicological effects of clozapine in adults may also occur in the fetus.

Flupenthixol C

When given in high doses during late pregnancy, related compounds have caused prolonged neurological disturbances in the newborn infant.

Lithium salts D

The risk of birth defects may be increased when lithium is used during the first trimester. Second trimester detailed ultrasound examination and fetal echocardiography should be considered for women who have been treated with lithium during the first trimester of pregnancy. The newborn may show signs of lithium toxicity.

Olanzapine, risperidone B3

Pimozide, thiothixene B1

Zuclopenthixol C

When given in high doses during late pregnancy, related compounds have caused prolonged neurological disturbances in the newborn infant.

CENTRAL NERVOUS SYSTEM

ANTIDEPRESSANTS

Selective serotonin reuptake inhibitors (SSRIs)

SSRIs have had limited use in pregnancy without a reported increase in birth defects. The use of SSRIs in the third trimester may result in a withdrawal state in the newborn infant.

Citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline — **C**

Tricyclic antidepressants

Withdrawal symptoms in newborn infants have been reported with prolonged maternal use of this class of drugs.

Amitriptyline, clomipramine, desipramine, dothiepin, doxepin, imipramine, nortriptyline, protriptyline, trimipramine — **C**

Tetracyclic antidepressants

Mianserin — **B2**

Monoamine oxidase inhibitors

Phenelzine — **B3**

Tranylcypromine — **B2**

OTHER ANTIDEPRESSANTS

Mirtazapine, moclobemide, nefazodone — **B3**

Venlafaxine — **B2**

CNS STIMULANTS

Caffeine — **A**

Dextroamphetamine — **B3**

Methylphenidate — **B2**

ANTIPARKINSON AGENTS

Amantadine, apomorphine, benserazide, carbidopa, entacapone, levodopa, ropinirole, **B3**

Benztropine, biperiden, selegiline **B2**

Benzhexol **B1**

Pergolide **C**

Studies in rodents have shown no evidence of harm to the fetus. There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Procyclidine **A**

ANTICONVULSANTS / ANTIEPILEPTICS

The risk of having an abnormal child as a result of antiepileptic medication is far outweighed by the dangers to the mother and fetus of uncontrolled epilepsy.

It is recommended that:

- *women on antiepileptic drugs (AEDs) receive prepregnancy counselling with regard to the risk of fetal abnormalities;*
- *AEDs should be continued during pregnancy and monotherapy should be used if possible at the lowest effective dose as risk of abnormality is greater in women taking combined medication;*
- *folic acid supplementation (5mg) should be commenced four weeks prior to and continue for twelve weeks after conception;*
- *Specialist prenatal diagnosis including detailed mid-trimester ultrasound should be offered.*

CENTRAL NERVOUS SYSTEM

Commonly Prescribed Anticonvulsants/Antiepileptics

Carbamazepine **D**

Spina bifida occurs in about one percent of pregnancies in which carbamazepine is used as monotherapy. Carbamazepine taken during pregnancy also has been associated with minor craniofacial defects, fingernail hypoplasia and developmental disability. Carbamazepine also can cause coagulation defects with consequent risk of haemorrhage in the fetus and the newborn infant which may be preventable by the prophylactic administration of vitamin K to the mother prior to delivery.

Phenytoin sodium **D**

This drug taken during pregnancy has been associated with craniofacial defects, fingernail hypoplasia, developmental disability, growth retardation and less frequently, oral clefts and cardiac anomalies. This clinical pattern is sometimes called the 'fetal hydantoin syndrome'. Phenytoin also can cause coagulation defects with consequent risk of haemorrhage in the fetus and the newborn infant which may be preventable by the prophylactic administration of vitamin K to the mother prior to delivery.

Methylphenobarbitone, phenobarbitone, primidone **D**

The use in pregnancy of primidone, phenobarbitone or methylphenobarbitone has been associated with minor craniofacial defects, fingernail hypoplasia and developmental disability. Their use in pregnancy alone, or in combination with other anticonvulsants, can cause coagulation defects in the newborn infant which may be preventable by the prophylactic administration of vitamin K to the mother prior to delivery.

Sodium valproate (valproic acid) **D**

If taken in the first trimester of pregnancy, sodium valproate (valproic acid) is associated with a one to two percent risk of neural tube defects (especially spina bifida) in the exposed fetus. Women taking sodium valproate (valproic acid) who become pregnant should be encouraged to consider detailed mid-trimester morphology ultrasound for prenatal diagnosis of such abnormalities.

Other anticonvulsants / antiepileptics

Compared to conventional anticonvulsants, the extent of the risk of the following drugs is unknown.

Clonazepam **C**

Clonazepam is a benzodiazepine. These drugs may cause hypotonia, respiratory depression and hypothermia in the newborn infant if used in high doses during labour. Withdrawal symptoms in newborn infants have been reported with this class of drugs.

Ethosuximide, methsuximide, phensuximide, sulthiame, vigabatrin **D**

Gabapentin **B1**

Lamotrigine, tiagabine, topiramate **B3**

CENTRAL NERVOUS SYSTEM

ANTIEMETICS, ANTINAUSEANTS

Phenothiazines

When given in high doses during late pregnancy, phenothiazines have caused prolonged neurological disturbances in the infant.

Prochlorperazine, promethazine, thiethylperazine	**C**

OTHERS

Dimenhydrinate, diphenhydramine, metoclopramide	**A**
Dolasetron, granisetron, ondansetron	**B1**
Domperidone, hyoscine, hyoscine hydrobromide	**B2**
Tropisetron	**B3**

OTHER AGENTS ACTING ON THE CNS

Tetrabenazine	**B2**

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

(See also analgesics, antipyretics page 13)

These agents inhibit prostaglandin synthesis and, when given during the latter part of pregnancy, may cause closure of the fetal ductus arteriosus, fetal renal impairment, inhibition of platelet aggregation, and delay labour and birth. Continuous treatment with NSAIDs during the last trimester of pregnancy should only be given on sound indications. During the last few days before expected birth, agents with an inhibitory effect on prostaglandin synthesis should be avoided.

Diclofenac, diflunisal, ibuprofen, indomethacin, ketoprofen, ketorolac, mefenamic acid, nabumetone, naproxen, phenylbutazone, piroxicam, sodium salicylate, sulindac, tenoxicam, tiaprofenic acid C

ANTIRHEUMATOID AGENTS

Aurothioglucose, sodium aurothiomalate, B2

Auranofin B3

Hydroxychloroquine D

When used in high doses and for prolonged periods, chloroquine and related substances may cause neurological disturbances and interference with hearing, balance and vision in the fetus.

Penicillamine D

This drug can cause cutis laxa in the human fetus.

MUSCLE RELAXANTS

Baclofen, botulinum type A B3

Dantrolene, methocarbamol, orphenadrine, B2

Physostigime C

Quinine **D**

At standard doses, quinine has not been associated with fetal damage. In toxic doses, quinine causes fetal damage including deafness. Its ability to induce uterine contractions also constitutes a risk of abortion.

AGENTS USED IN GOUT AND HYPERURICAEMIA

Allopurinol, colchicine, probenecid, sulfinpyrazone **B2**

OESTROGENS (SEE ORAL CONTRACEPTIVES)

Dienoestrol	**X**
Ethinyloestradiol, mestranol	**B3**
Oestradiol, oestriol, oestrone, piperazine oestrone sulfate	**B1**
Oestrogens conjugated	**D**

PROGESTOGENS (SEE ORAL CONTRACEPTIVES)

If taken by the mother at or after 8 weeks post conception, these drugs can cause virilisation of the female fetus. This is a dose-dependent effect. Prior to 8 weeks post conception, they have no virilising effects.

Dydrogesterone, hydroxyprogesterone, megestrol, norethisterone	**D**
Medroxyprogesterone (oral high dose, 30-50mg daily) (see also contraceptives and anti-neoplastic agents)	**D**

ANTIANDROGENS

Antiandrogens carry the potential for feminisation of the male fetus at or after 8 weeks post conception and should be avoided during pregnancy.

Cyproterone acetate, spironolactone	**B3**

ANDROGENS AND ANABOLIC STEROIDS

Anabolic steroids and other substances with androgenic effects may have a virilising effect on the female fetus and should be avoided during pregnancy.

Fluoxymesterone, methenolone, nandrolone, oxandrolone, oxymetholone, testosterone	**D**

ENDOCRINE SYSTEM

CORTICOSTEROIDS

Systemic

Betamethasone, cortisone, dexamethasone, fludrocortisone, hydrocortisone, methylprednisolone, prednisolone, prednisone, triamcinolone — **A**

Topical

Betamethasone, fludrocortisone, flumethasone, fluocinolone, fluocortolone, halcinonide, triamcinolone — **A**

Methylprednisolone aceponate — **C**

Mometasone — **B3**

Inhalation/Intranasal

The benefits of asthma control outweigh any potential for an adverse pregnancy outcome.

Beclomethasone, flunisolide, fluticasone, triamcinolone — **B3**

Budesonide — **A**

PITUITARY HORMONES

Corticotrophin — **A**

Nafarelin, goserelin — **D**

There is a theoretical risk of abortion or fetal abnormality if GnRH agonists are used during pregnancy.

Somatropin, thyrotrophin — **B2**

ANTIDIURETICS

Desmopressin, lypressin, vasopressin — **B2**

HYPOGLYCAEMIC AGENTS (ORAL)

It is important to achieve strict normoglycaemia during pregnancy. This may best be achieved by conversion to insulin therapy.

Acarbose, miglitol — **B3**

Chlorpropamide, glibenclamide, gliclazide, glimepiride, glipizide, metformin, tolazamide, tolbutamide — **C**

The sulphonylureas may enter the fetal circulation and may cause neonatal hypoglycaemia.

THYROID HORMONES

Liothyronine, thyroxine — **A**

ANTITHYROID AGENTS

These agents may cause congenital goitre by inhibiting thyroxine synthesis in the fetus.

Carbimazole, propylthiouracil — **C**

AGENTS AFFECTING CALCIUM AND BONE METABOLISM

Alendronate, clodronate, pamidronate — **B3**

Calcitonin, salcatonin, tiludronate disodium — **B2**

Calcitriol, dihydrotachysterol — **B3**

Raloxifene — **X**

This drug causes abnormalities of the developing reproductive system when administered to pregnant rabbits and may have a similar effect in human pregnancy.

OTHER HORMONAL AGENTS

Aminoglutethimide D

There have been reports of pseudohermaphrodism with use of this drug in pregnancy.

Octreotide C

This drug may produce fetal growth retardation, probably due to suppression of growth hormone.

PITUITARY INHIBITORS

Bromocriptine (oral) A

Bromocriptine (injection) B2

Cabergoline B1

Danazol D

If taken by the mother at or after 8 weeks post conception, danazol may cause virilisation of the female fetus. Prior to 8 weeks post conception it has no virilising effects. Danazol may not inhibit ovulation in all women.

Gestrinone D

This drug may interfere with pregnancy and in animal tests caused masculinisation of female fetuses. Gestrinone may not inhibit ovulation in all women.

Quinagolide B3

OVULATION INDUCERS

Gonadotrophins

Human chorionic gonadotrophin A

Human menopausal gonadotrophin, urofollitrophin B2

Recombinant follicle stimulating hormone (FSH) B3

Clomiphene B3

URINARY ANTISEPTICS

Hexamine A

BLADDER FUNCTION DISORDERS

Bethanechol B2

Bethanechol has a potent excitatory effect on smooth muscle and should be avoided during pregnancy.

Finasteride X

Finasteride may cause abnormalities of the external genitalia of a male fetus.

Oxybutynin, pentosan polysulfate sodium B1

Terazosin B2

AGENTS ACTING ON THE UTERUS

Ergometrine C

This drug induces uterine contraction and may cause premature or hypertonic labour. Products containing ergometrine should be avoided during pregnancy.

Gemeprost B3

Oxytocin A

There have been instances of idiosyncratic sensitivity of the uterus resulting in fetal anoxia.

Prostaglandin E2/Dinoprostone C

There have been instances of idiosyncratic sensitivity of the uterus resulting in fetal anoxia.

Salbutamol A

TOPICAL VAGINAL MEDICATION

CEPHALOSPORINS

Cefaclor , cefotaxime, cefotetan, cefoxitin, cefpodoxime, ceftazidime, ceftriaxone, cephamandole, cephazolin	**B1**
Cefodizime, cefpirome	**B2**
Cephalexin, cephalothin	**A**

PENICILLINS

Amoxycillin, ampicillin, benzathine penicillin, benzylpenicillin, phenoxymethylpenicillin, procaine penicillin	**A**
Amoxycillin with clavulanic acid, flucloxacillin, mezlocillin, piperacillin, piperacillin with tazobactam	**B1**
Azlocillin	**B3**
Dicloxacillin, ticarcillin sodium with potassium clavulanate	**B2**

TETRACYCLINES

Tetracyclines are safe for use during the first 18 weeks of pregnancy (16 weeks post conception) after which they cause discolouration of the baby's teeth.

Demeclocycline, doxycycline, minocycline, tetracycline	**D**

AMINOGLYCOSIDES

There is evidence of selective uptake of aminoglycosides by the fetal kidney resulting in damage (probably reversible) to immature nephrons. Eighth cranial nerve damage has also been reported following in utero exposure to some of the aminoglycosides. Because of their chemical similarity, all aminoglycosides must be considered potentially nephrotoxic and ototoxic to the fetus. It should also be noted that therapeutic blood concentrations in the mother do not equate with safety for the fetus.

Amikacin, gentamicin, kanamycin, neomycin, netilmicin, tobramycin	**D**

ANTIFUNGAL AGENTS *(See also topical antifungals page 46)*

Amphotericin B3

Fluconazole D

Single dose therapy (150mg) does not appear to cause adverse pregnancy effects. Repeated doses of fluconazole (400-800mg daily) have been associated with a consistent pattern of birth defects similar to those seen in animal studies.

Flucytosine, griseofulvin, itraconazole, ketoconazole B3

Terbinafine B1

Nystatin A

QUINOLONES

Alatrofloxacin, ciprofloxacin, enoxacin, fleroxacin, norfloxacin, ofloxacin B3

MACROLIDE ANTIBIOTICS

Azithromycin, roxithromycin B1

Clarithromycin B3

Erythromycin A

MISCELLANEOUS ANTIBIOTICS

Atovaquone, colistin IV , meropenem, metronidazole, vancomycin B2

Aztreonam, mupirocin, spectinomycin B1

Chloramphenicol, clindamycin, lincomycin, nalidixic acid A

Clavulanic acid B1

Fusidic acid C

This drug may cause kernicterus in babies during the first month of life by displacing bilirubin from plasma albumin. Fusidic acid should be avoided if possible during the last month of pregnancy.

Imipenem-cilastatin combination, teicoplanin, tinidazole B3

Nitrofurantoin (short term therapy) A

Caution should be exercised when administering nitrofurantoin at term because of the possibility of producing haemolytic anaemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency and due to immature enzyme systems in the early neonatal period.

Pentamidine B3

Trimethoprim B3

SULFONAMIDES

Sulfonamides may cause jaundice and haemolytic anaemia in the newborn.

Sulfadoxine, sulfadiazine, sulfamethizole, sulfamethoxazole C

Trimethoprim-sulfonamide combinations C

ANTITUBERCULOTICS AND ANTILEPROTICS

Ethambutol, isoniazid A

Clofazimine C

Clofazimine may cause discolouration of the skin of the baby. This is reversible but recovery may be delayed because clofazimine has an average serum half life of 70 days.

Dapsone, pyrazinamide B2

Rifabutin C

Bleeding attributable to hypoprothrombinaemia has been reported in newborn infants and in mothers after the use of rifampicin during late pregnancy. If rifabutin is used during the last few weeks of pregnancy, vitamin K should be given to the mother and the newborn infant.

ANTIMICROBIALS

Rifampicin **C**

Bleeding attributable to hypoprothrombinaemia has been reported in newborn infants and in mothers after the use of rifampicin during late pregnancy. If rifampicin is used during the last few weeks of pregnancy, vitamin K should be given to the mother and the newborn infant.

ANTIMALARIALS

The use of these drugs in the treatment of malaria is accepted because the small risk to the fetus is outweighed by the benefits to the mother and fetus. Prophylaxis in high risk situations is also justified.

Chloroquine (prophylaxis) **A**

Chloroquine (treatment), hydroxychloroquine **D**

When used in high doses and for prolonged periods, chloroquine and related substances may cause neurological disturbances and interference with hearing, balance and vision in the fetus.

Doxycycline **D**

Tetracyclines are safe for use during the first 18 weeks of pregnancy (16 weeks post conception) after which they cause discolouration of the baby's teeth.

Mefloquine, pyrimethamine-dapsone combination **B3**

Primaquine phosphate **D**

Avoid use in third trimester as primaquine may cause neonatal haemolysis and methaemoglobinaemia.

Proguanil **B2**

If given during pregnancy, folic acid supplementation should be given. Proguanil has been used extensively with no adverse pregnancy outcome.

Pyrimethamine B3

This drug may interfere with folic acid metabolism and animal experiments have shown that administration of very high doses of pyrimethamine during organ development may give rise to birth defects typical of folic acid antagonism. If pyrimethamine is given during pregnancy, folic acid supplementation should be given.

Pyrimethamine-sulfadoxine combination C

Pyrimethamine may interfere with folic acid metabolism and if it is given during pregnancy folic acid supplementation should be given. Sulfonamides may cause jaundice and haemolytic anaemia in the newborn.

Quinine (treatment) D

In toxic doses, quinine causes fetal damage including deafness. Its ability to induce uterine contractions also constitutes a risk of abortion.

ANTIVIRAL AGENTS

Aciclovir , indinavir , ritonavir , valaciclovir B3

Cidofovir D

This drug could be expected to cause fetal loss and birth defects.

Delavirdine, foscarnet, lamivudine, nevirapine, stavudine, zidovudine B3

Didanosine B2

Famciclovir , saquinavir B1

Ganciclovir D

This drug has been shown to be teratogenic and embryotoxic in animals.

Nelfinavir B2

ANTIMICROBIALS

Ribavirin — **X**

Although there are no pertinent human data, ribavirin has been found to be teratogenic and/or embryolethal in nearly all species in which it has been tested. Malformations of skull, palate, eye, jaw, skeleton and gastrointestinal tract were noted in animal studies. Survival of fetuses and offspring was reduced.

Zalcitabine — **D**

This drug is teratogenic in two animal species.

ANTHELMINTICS

Albendazole — **D**

In animal studies albendazole is teratogenic in several species. Until human data are available, it must be suspected of being teratogenic.

Ivermectin, mebendazole, thiabendazole — **B3**

Praziquantel — **B1**

Pyrantel embonate, diethylcarbamazine — **B2**

Cytotoxic agents can pr oduce spontaneous abor tion, fetal loss and birth defects.

ALKYLATING AGENTS

Busulfan, carmustine, chlorambucil, cyclophosphamide, estramustine, fotemustine, ifosfamide, lomustine, melphalan, mustine, thiotepa **D**

ANTIMETABOLITES

Cladribine, colaspase, cytarabine, docetaxel, fluorouracil, gemcitabine, hydroxyurea, methotrexate, mercaptopurine, paclitaxel, raltitrexed, thioguanine, topotecan **D**

VINCA ALKALOIDS

V inblastine, vincristine, vindesine, vinorelbine tartrate **D**

ANTIBIOTIC CYTOTOXIC AGENTS

Bleomycin, dactinomycin, daunorubicin, doxorubicin, epirubicin, fludarabine, idarubicin, mitomycin, mitozantrone **D**

HORMONAL ANTINEOPLASTIC AGENTS

Aminoglutethimide **D**

There have been reports of pseudohermaphrodism with use of this drug in pregnancy.

Anastrozole **C**

This drug disrupts oestrogen dependent metabolism and may result in abortion.

Goserelin, letrozole, leuprorelin **D**

There is a theoretical risk of abortion or fetal abnormality if GnRH agonists are used during pregnancy.

ANTINEOPLASTIC AGENTS

Medroxyprogesterone (oral and IM high dose) **D**

May cause virilisation of fetus if taken 8 weeks after conception.

Tamoxifen, toremifene **B3**

OTHER ANTINEOPLASTIC AGENTS

Altretamine, amsacrine, carboplatin, cisplatin, dacarbazine, etoposide, irinotecan, procarbazine, samarium[^{153} Sm], teniposide **D**

Tretinoin (Oral) **X**

This is a potent teratogen when taken systemically during early preganancy, producing a pattern of birth defects termed retinoic acid embryopathy. The teratogenic effect is dose-dependent.

NON-CYTOTOXIC SUPPORTIVE THERAPY

Amifostine **B3**

Mesna **B1**

ANORECTIC AND WEIGHT REDUCING AGENTS

Weight reduction using appetite suppressant drugs is not recommended in pregnancy.

Dexfenfluramine, mazindol, phentermine B3

Diethylpropion, fenfluramine B2

OTHER DRUGS USED FOR THE TREATMENT OF METABOLIC DISORDERS

Alglucerase, cysteamine bitartrate B3

ANTITUSSIVES

Opium alkaloids and derivatives: codeine, dextromethorphan, dihydrocodeine, pholcodine — **A**

EXPECTORANTS AND MUCOLYTICS

Acetylcysteine (inhaled) — **B2**

Ammonium chloride, bromhexine, emetine, guaiphenesin, ipecacuanha, saponins — **A**

DECONGESTANTS

Phenylephrine, phenylpropanolamine, pseudoephedrine — **B2**

INHALATIONAL AGENTS

The agents that contain norflurane as the propellant have had limited human exposure. Norflurane has been shown to be safe in animals. The prescriber should consult the full pi for more information.

Bronchospasm relaxants

Eformoterol, salmeterol — **B3**

Ephedrine, fenoterol, isoprenaline, orciprenaline, rimiterol, salbutamol, terbutaline, theophylline derivatives — **A**

Ipratropium bromide — **B1**

Preventive aerosols and inhalations

Beclomethasone, budesonide, fluticasone, salmeterol — **B3**

The benefits of asthma control outweigh any potential for an adverse pregnancy outcome.

Nedocromil — **B1**

Sodium cromoglycate — **A**

OTHER RESPIRATORY AGENTS

ANTIHISTAMINES

Azatadine, cetirizine, diphenylpyraline, fexofenadine, methdilazine, terfenadine — **B2**

Brompheniramine, chlorpheniramine, clemastine,cyproheptadine, dexchlorpheniramine, diphenhydramine, diphenylamine, doxylamine, pheniramine, triprolidine — **A**

Chlorcyclizine, cyclizine, hydroxyzine — **A**

Levocabastine — **B3**

Inadvertent short term exposure during the first trimester is unlikely to cause a hazard to the fetus but it has been shown to be teratogenic in two species of animals and until human data are available, it should be suspected of being teratogenic.

Loratadine — **B1**

Trimeprazine, promethazine — **C**

When given in high doses during late pregnancy, phenothiazines have caused prolonged neurological disturbances in the infant.

VACCINES

LIVE ATTENUATED VIRUS VACCINES

Currently available live virus vaccines have not caused teratogenic effects in humans. The NHMRC publication, The Australian Immunisation Procedures Handbook, should be consulted for more comprehensive information.

B.C.G., measles, measles-mumps, measles-mumps-rubella, mumps, typhoid (oral), yellow fever — **B2**

Poliomyelitis (oral), typhoid (injection) — **A**

Rubella **B2**

Women of child bearing age should be tested for rubella antibodies prior to pregnancy. All seronegative women, provided they are not pregnant, should be offered rubella vaccine. Those administering the vaccine should be careful to instruct women to whom it is given that they should not become pregnant for at least two full menstrual cycles because rubella vaccine can cause fetal infection. However, to date, there have not been any rubella-like birth defects in the live born infants (about 400) of seronegative mothers vaccinated during or just before pregnancy. Based on this experience, rubella vaccination during pregnancy need not be the reason to recommend interruption of pregnancy.

KILLED VACCINES

Cholera, haemophilus influenzae type B, hepatitis A, hepatitis B, influenza, meningococcal, pneumococcal, poliomyelitis (injection) **B2**

Diphtheria, tetanus **A**

Rabies vaccine **B2**

The benefit clearly outweighs the risk for post exposure situations.

IMMUNOMODIFIERS

Azathioprine **D**

This drug has been associated with a slightly increased risk of fetal malformations, neonatal immunosuppression and bone marrow suppression in the infant.

Cyclosporin **C**

This drug may cause immunosuppression in the infant.

Interferon alpha-2a, interferon alpha-2b, interferon gamma-1b **B3**

ALLERGY AND IMMUNE SYSTEM

Interferon beta-1a **D**

Interferon beta-1a has abortifacient activity in monkeys.

Interferon beta-1b **D**

This drug has abortifacient activity in monkeys. Spontaneous abortions have been reported in subjects with multiple sclerosis in controlled clinical trials.

Levamisole **B3**

Mycophenolate mofetil **D**

Mycophenolate has been shown to be teratogenic in two species of animals. It inhibits nucleic acid synthesis and may cause fetal malformations/death.

Rituximab **C**

Antibodies of this class are known to cross the fetoplacental barrier and may cause B cell depletion and/or other unknown effects.

Tacrolimus **C**

This drug may cause immunosuppression in the infant. Use of tacrolimus during pregnancy has been associated with neonatal hyperkalaemia and renal dysfunction.

Benzydamine (topical oropharyngeal) B2

OPHTHALMIC DRUGS

Acetazolamide, apraclonidine, dorzolamide, latanoprost, levocabastine — **B3**

Betaxolol, levobunolol, timolol — **C**

Beta-adrenergic blocking agents may cause pharmacological effects such as bradycardia in the fetus and newborn infant.

Brimonidine tartrate, Iodoxamide trometamol — **B1**

Chloramphenicol — **A**

Ecothiopate — **B2**

Flurbiprofen — **B2**

Idoxuridine — **B3**

SYSTEMIC

Acitretin, etretinate — **X**

These drugs are teratogenic at doses within the therapeutic range. They are stored in the body for several months after cessation. Because of the long half-life of these drugs and storage in fat, patients are advised not to conceive until two years after cessation of treatment because of risk of birth defects. Should pregnancy occur during treatment with these drugs, there is a high risk of birth defects.

Isotretinoin — **X**

Isotretinoin is teratogenic and must not be used by females who are pregnant or who may possibly become pregnant while undergoing treatment and for one month after isotretinoin has stopped. Should pregnancy occur during treatment with this drug, there is a high risk of birth defects (refer to current Product Information).

TOPICAL

Adapalene — **D**

There have been isolated reports of birth defects in babies born to women using this drug. Because of the potential risk of adverse effects on fetal development, adapalene should not be used by women who are pregnant or who plan to become pregnant during treatment.

Azelaic acid, calcipotriol — **B1**

Desonide — **B3**

Finasteride — **X**

Finasteride may cause abnormalities of the external genitalia of a male fetus.

Isotretinoin D

Isotretinoin is known to be teratogenic when administered orally in human beings. It is associated with major birth defects and with a small risk of spontaneous abortion.

Methoxsalen B2

Tretinoin D

Use of tretinoin cream formulation during the first trimester does not appear to cause birth defects. Other formulations should not be used during pregnancy. There have been isolated reports of birth defects in babies born to women using topical tretinoin in pregnancy, some similar to those reported with oral retinoids. While a retrospective cohort study on women exposed to tretinoin in the first trimester did not reveal an association with this treatment, the numbers in this study are too small to establish the safety of use in pregnancy.

TOPICAL ANTIFUNGALS, ANTISEPTICS

Amorolfine, bifonazole, B3

Cetylpyridinium, chlorhexidine, chlorquinaldol, clotrimazole, econazole, hydroxyquinoline, miconazole A

TOPICAL ANTIPARASITICS

Benzyl benzoate, bioallethrin, crotamiton, maldison (malathion), permethrin, pyrethrins B2

Lindane B3

Lindane penetrates human skin and has been reported to cause signs of CNS irritation. Because of this toxic potential it is preferable, whenever possible, to use other medications during pregnancy.

Piperonyl butoxide B3

TOPICAL ANTIVIRAL

DRUGS USED IN ANAESTHESIA

GENERAL ANAESTHETICS

All general anaesthetics carry the potential to produce central nervous system and respiratory depression in the newborn infant. In routine practice this does not appear to be a problem. However, in the compromised fetus, careful consideration should be given to this potential depression and to the selection of particular anaesthetic drugs, doses and techniques.

Enflurane, halothane, ketamine, thiopentone — **A**

Desflurane, isoflurane — **B3**

Methohexitone, sevoflurane — **B2**

Methoxyflurane — **C**

Nitrous oxide — **A**

Propofol — **C**

LOCAL ANAESTHETICS

Bupivacaine, cinchocaine, lignocaine, mepivacaine, prilocaine — **A**

Etidocaine, ropivacaine — **B1**

Procaine hydrochloride — **B2**

NEUROMUSCULAR BLOCKING AGENTS

Alcuronium, mivacurium, pancuronium, rocuronium — **B2**

Atracurium, gallamine, pipecuronium, tubocurarine, vecuronium — **C**

There have been no demonstrated adverse effects in the fetus or the newborn infant.

Suxamethonium — **A**

Medroxyprogesterone (IM contraceptive dose) **A**

ORAL CONTRACEPTIVES

Combined, progestogen only **B3**

Accumulated evidence reports that inadvertent exposure to these agents in early pregnancy has not been associated with an increased risk of birth defects.

VAGINAL SPERMICIDES

Nonoxynol 9, octoxinol **A**

DIAGNOSTIC AGENTS

If a radiological contrast or other diagnostic agent is not in this booklet refer to the product information or contact an obstetric drug information service (see Appendix B).

RADIOGRAPHIC AGENTS

Ioversol B1

Gadodiamide, iomeprol B3

Galactose and palmitic acid B2

PITUITARY-ADRENAL RESPONSE TEST

Metyrapone B2

Tetracosactrin D

There have been some reports of miscarriage or fetal malformation occurring in pregnant women treated with tetracosactrin.

DETOXIFYING AGENTS, ANTIDOTES

Acetylcysteine (intravenous), digoxin immune fab — **B2**

Desferrioxamine, flumazenil — **B3**

Naloxone — **B1**

Penicillamine — **D**

Penicillamine can cause cutis laxa in the human fetus.

CHOLINERGIC AND ANTICHOLINERGIC AGENTS

Atropine, hyoscine methobromide, papaverine — **A**

Atropine methonitrate, belladonna, glycopyrrolate, hyoscine, hyoscine-N-butylbromide, hyoscyamine, propantheline — **B2**

Bethanechol — **B2**

This drug has a potent excitatory effect on smooth muscle and should be avoided during pregnancy.

Donepezil — **B3**

Tacrine — **C**

This drug may produce cholinergic effects in the fetus.

DRUGS USED IN MYASTHENIA GRAVIS

Ambenonium chloride, neostigmine — **B2**

Pyridostigmine — **C**

The maternal requirement for this drug in the context of myasthenia gravis may be absolute. Cholinergic effects in the neonate are rare.

AGENTS USED IN DEPENDENCY STATES

Calcium carbimide — **A**

Disulfiram — **B2**

MISCELLANEOUS

Methadone — **C**

Narcotic analgesics may cause respiratory depression in the newborn infant. Withdrawal symptoms in newborn infants have been reported with prolonged use of this drug.

Naltrexone — **B3**

Nicotine — transdermal — **D**

— in chewing gum — **D**

The harmful effects of cigarette smoking on maternal and fetal health are clearly established. The specific effects of nicotine therapy on fetal development are unknown. Short-term exposure during the first trimester is unlikely to cause a hazard to the fetus.

VITAMINS

Nicotinic acid — **B2**

Vitamin A — **D**

Excess vitamin A may cause birth defects. Women should consider their dietary intake of vitamin A before taking supplements. The Australian diet usually contains the recommended daily allowance of 2500 IU.

INDEX

INDEX

Therapeutic goods exempted from pregnancy classification

The following classes of therapeutic goods have not been generally included in this categorisation. There are, however, some therapeutic goods within these classes which have been assigned a pregnancy classification at registration and have been listed in the text.

- Antiflatulents (silicones)
- Antigen preparations for desensitisation
- Antihaemorrhagics: antifibrinolytics, fibrinogen, blood coagulation factors
- Certain anti-poisoning agents: potassium iodide
- Topical antirheumatics
- Antivenoms & antitoxins
- Charcoal preparations
- Contact lens preparations
- Diagnostic agents (urinalysis agents, ocular staining agents etc.)
- Digestives, including enzymes
- Ear preparations for topical use
- Enzymes (haematological), including fibrinolytics and hyaluronidase
- Topical preparations for haemorrhoids, except those containing corticosteroids
- Herbal medicines

APPENDIX A

- Hormones that are indicated only for termination of pregnancy, postmenopausal substitution therapy, male hypogonadism, amenorrhoea, cystic glandular hyperplasia, or prostatic cancer
- Infant formulas
- Insulins and glucagon
- Keratolytics, cleansers, bath additives
- Certain laxatives: lactulose, bulk producers and enemas
- All medical devices (including prostheses, surgical implants, ostomy aids, surgical dressings, contraceptive devices, etc.)
- Mineral supplements
- Mouth preparations excluding those containing benzydamine
- Topical nasal decongestants, sympathomimetics and combinations excluding steroids
- Nutritional supplements
- Ocular irrigants
- Topical organoheparinoids
- Parenteral nutrition preparations
- Plasma substitutes and intravenous solutions, including solutions for intravenous feeding
- Scabicides, except when containing DDT, lindane or maldison (malathion)
- Sera and gammaglobulins
- Urinary sediment solvents
- Varicose vein therapies
- Vitamins (other than vitamin A and nicotinic acid)
- Zinc bandages

Obstetric Drug Information Services

The following services are available to health professionals.

AUSTRALIAN CAPITAL TERRITORY

A.C.T. Drug Information Service
Woden Valley Hospital
Garran ACT 2605

Phone: (02) 6244 3333
Fax: (02) 6244 3334

NEW SOUTH WALES

Pregnancy and Neonatal Drug Advisory Service
Poisons Information Centre
The New Children's Hospital
Hawksbury Road
Westmead NSW 2148

Phone: (02) 9845 3111
131126
Fax: (02) 9845 3597

VICTORIA

Royal Women's Hospital
Obstetric Drug Information Centre
132 Grattan Street
Carlton VIC 3053

Phone: (03) 9344 2277
Fax: (03) 9349 2756

APPENDIX B

Monash Medical Centre
Obstetric Drug Information
246 Clayton Road
Clayton VIC 3168

Phone: (03) 9594 2361
Fax: (03) 9594 2595

SOUTH AUSTRALIA

Drugs in Pregnancy and Lactation Information Service
Women's and Children's Hospital
72 King William Road
North Adelaide SA 5006

Phone: (08) 8204 7555
Fax: (08) 8204 6049

WESTERN AUSTRALIA

Obstetric Drug Information Service
King Edward Memorial Hospital for Women
374 Bagot Road
Subiaco WA 6008

Phone: (08) 9340 2723
Fax: (08) 9340 2713

QUEENSLAND

Royal Women's Hospital
Obstetric Drug Information Service
Brisbane QLD

Phone: (07) 3253 7300
Fax: (07) 3253 3544

Queensland Drug Information Centre
Royal Brisbane Hospital
E Floor, Block 7
Herston Road
Herston QLD 4029

Phone: (07) 3253 7098
(07) 3253 7599
Fax: (07) 3253 1393

TASMANIA

Drug Information Centre
Pharmacy Department
Royal Hobart Hospital
GPO Box 1061L
Hobart TAS 7001

Phone: (03) 6238 8737
Fax: (03) 6222 8029 or (03) 6231 2905

NORTHERN TERRITORY

Northern Territory Drug Information Centre
Royal Darwin Hospital
PO Box 41 326
Casuarina NT 0811

Phone: (08) 8922 8424
Fax: (08) 8922 8499