

Guidelines for the Use of Mifepristone for Medical Abortion in New Zealand

Contents

Abbreviations used in this document.....	6
1. Introduction.....	7
2. Background.....	7
2.1 Approval of mifepristone (Mifegyne®) in New Zealand.....	7
2.2 Legal requirements.....	7
3. Second Trimester Abortion.....	8
3.1 Background.....	8
3.2 Mifepristone dosage.....	8
3.3 The prostaglandin.....	8
3.4 Interval between mifepristone and the prostaglandin.....	9
3.5 Second trimester protocols.....	9
4. First Trimester Medical Abortion.....	10
4.1 Background.....	10
4.2 Gestational age.....	10
4.2.1 Registered use.....	10
4.2.2 49-63 days' gestation.....	10
4.2.3 9-13 weeks' gestation.....	11
4.2.4 Early pregnancy with no visualised sac.....	11
4.2.5 Summary.....	11
4.3 The method.....	11
4.3.1 Mifepristone dosage.....	11
4.3.2 Interval between mifepristone and misoprostol.....	11
4.3.3 The prostaglandin – misoprostol or gemeprost.....	12
4.3.4 Route of administration of misoprostol.....	12
4.3.5 Dose of misoprostol.....	12
4.3.6 Informed consent.....	12
4.4 Management in clinic or at home.....	13
4.4.1 After mifepristone administration.....	13
4.4.2 After misoprostol administration.....	13
4.4.3 Assessment of patients for early discharge after misoprostol.....	13
4.4.4 Clinic ability to support patient at home.....	14
4.5 Medical follow-up after first trimester medical abortion.....	14
4.5.1 Evidence.....	14
4.5.2 Recommendations for follow-up.....	14
4.5.3 Use of β hCG and USS for follow-up.....	15

4.5.4	Follow-up of women who fail to attend appointments.....	16
4.5.5	Specialist follow-up of complications of medical abortion.....	16
4.6	Patient acceptability.....	16
4.7	Management of pain.....	17
4.7.1	Non-medical pain management strategies.....	17
4.7.2	Analgesia.....	18
4.8	Back-up medical services.....	18
5.	Drugs – Actions, Interactions and Contraindications.....	19
5.1	Drug names.....	19
5.2	Drug actions.....	19
5.3	Presentation and storage.....	19
5.4	Cost of the drugs.....	19
5.5	Contraindications to mifepristone / prostaglandin abortion.....	19
5.5.1	Absolute contraindications.....	19
5.5.2	Relative contraindications.....	19
5.6	Side effects.....	20
5.6.1	After mifepristone administration.....	20
5.6.2	After misoprostol administration.....	20
6.	Model Process for First Trimester Medical Abortions.....	22
6.1	Patient referral.....	22
6.2	Client profile.....	22
6.3	First clinic visit – Day 1.....	22
6.3.1	Counselling.....	23
6.3.2	Medical assessment.....	23
6.3.3	Nurse/midwife care.....	24
6.3.4	Administration of the treatment.....	24
6.3.5	Support for patient at home during interval between mifepristone and misoprostol.....	24
6.4	Second clinic visit – Day 2.....	25
6.4.1	Discharge home immediately after misoprostol administration.....	25
6.4.2	Patient remaining in clinic after misoprostol administration.....	25
6.4.3	Analgesia.....	26
6.4.4	Possible complications.....	26
6.4.5	Failure to complete under clinic observation.....	26
6.5	Final medical consultation to ensure abortion is complete.....	26
7.	Premises and Facilities.....	27
7.1	In the clinic.....	27
7.2	At home.....	28
7.3	Ultrasound.....	28
7.4	Written materials.....	28

8. Staffing and Staff Training.....	29
8.1 Staffing levels.....	29
8.2 Provider acceptability.....	29
8.3 Role of nurse/midwife.....	29
8.4 Staff training for medical abortion.....	30
8.4.1 Introduction.....	30
8.4.2 Training for referring agencies.....	31
8.4.3 Administrative staff.....	31
8.4.4 Training for counsellors.....	31
8.4.5 Medical staff training.....	32
8.4.6 Nurse/midwife training.....	32
8.4.7 Training for specialist services.....	32
8.4.8 Training for second trimester services.....	32
9. Counselling for Medical Abortion.....	34
9.1 General.....	34
9.2 Social factors.....	34
9.3 Support.....	35
9.4 Psychological and emotional factors.....	35
9.5 Second trimester abortions.....	35
9.6 Other issues.....	36
10. Management of Fetal Tissue.....	37
11. Evaluation and Audit.....	38
11.1 Audit in the clinic.....	38
11.2 National audit.....	38
11.3 Abortion Supervisory Committee.....	38
12. Resources.....	39
References	40
Appendix 1 - Data Sheet- Mifegyne 200 Mg	
Appendix 2 - Istar Limited	
Appendix 3 - Sample Consent Forms	
Appendix 4 - On-Call Medical Abortion Telephone Assessment Guide	
Appendix 5 - General Guide for initiation of Medical Abortion Services	
Appendix 6 - Sample Patient Information Pamphlets	
Appendix 7 - Information For Referring Doctors	
Appendix 8 - Management Of Side Effects And Complications Of Early Medical Termination of Pregnancy	
Appendix 9 - Level J Unit Client Information Sheet – Pregnancy Tissue	

Abbreviations used in this document

βhCG	beta human chorionic gonadotrophin
ASC	Abortion Supervisory Committee
CS & A Act	Contraception, Sterilisation, and Abortion Act 1977
BPAS	British Pregnancy Advisory Service
IUCD	intrauterine contraceptive device
NSAID	Non-steroidal anti-inflammatory drug
RCOG	Royal College of Obstetricians and Gynaecologists
RPOC	retained products of conception
TOP	Termination of pregnancy
USS	Ultrasound scan

1. Introduction

In May 2003 the Abortion Supervisory Committee (ASC) appointed a technical committee to advise it on the use of mifepristone for medical abortion in New Zealand. The technical committee was asked to develop guidelines and report back within three months.

The members of the technical committee were Miss Vasudha Iyengar, Ms Hazel Irvine and Dr Carol Shand*. Mr John Tait provided additional advice during Miss Iyengar's absence overseas. They sought input from Annie Muirgen, Senior Social Worker at the Level J Unit, and Janet Campbell, counselling advisor to the ASC.

The aim of these guidelines is to provide information to ensure the provision of **clinically safe, evidence-based medical abortion that meets New Zealand legal requirements and is cost-effective.**

2. Background

2.1 Approval of mifepristone (Mifegyne®) in New Zealand

In March 2001 the Medicines Advisory Committee recommended that Mifegyne® be approved under Section 21 of the Medicines Act 1981 for use in the following indications:

- *As a medical alternative to surgical termination of intra-uterine pregnancy*
- *Softening and dilation of the cervix uteri prior to surgical termination of intra-uterine pregnancy*
- *Preparation for the action of prostaglandin analogues in the termination of pregnancy for medical reasons*
- *Labour induction for the expulsion of a dead foetus (foetal death in utero)*

Mifegyne® was gazetted for use in New Zealand in August 2001 (see Appendix 1, Mifegyne® data sheet).

Mifegyne® is manufactured in France for Exelgyn and imported into New Zealand by a not-for-profit company, Istar Limited. See Appendix 2 for information on how to order supplies.

Where possible in this document the generic names of drugs will be used, i.e. Mifegyne® will be referred to by its generic name, mifepristone.

2.2 Legal requirements

For the purposes of this clinical document, compliance with the legal requirements of abortion is assumed.

* Miss Vasu Iyengar, MBS, MRCOG, FRANZCOG, CCT Obstetrician and Gynaecologist, Capital & Coast District Health Board

Ms Hazel Irvine, NZRGON, NZRM, MNZAP, Service Leader Level J Unit, Capital & Coast District Health Board

Dr Carol Shand, MB, ChB, FACSH, FRNZCGP, General Practitioner and Sexual Health Physician, Operating doctor Level J Unit, Capital & Coast District Health Board, Director Istar Ltd.

3. Second Trimester Abortion

3.1 Background

Late mid-trimester medical termination of pregnancy with mifepristone followed by the prostaglandin misoprostol is now the most commonly used method in six of the larger units in New Zealand. The experience of these units is very positive and both client and provider satisfaction are anecdotally reported. This confirms overseas experience.

Because the most commonly used method, in New Zealand, for second trimester abortion (over 16 weeks) has been induction with a prostaglandin, it is simple to add mifepristone to this regime. It provides real advantages to both the women and the providers:

- The interval between the administration of the prostaglandin and delivery of the products is shortened from an average of 15.8 hours to 6.8 hours (Rodger and Baird 1990; Urquhart and Templeton 1990).
- The amount of prostaglandin required is reduced.
- The cost of the procedure is consequently reduced despite the added cost of mifepristone.
- The shortened time reduces the psychological stress on both the women and the staff.

3.2 Mifepristone dosage

The dose of mifepristone recommended in the data sheet and in early trials is 600 mg. More recent published experience suggests that this can be reduced to 200 mg (Webster, Penney et al. 1996). The Royal College of Gynaecologists (RCOG 2000) in their evidence-based guidelines state that a dose of 200 mg is adequate.

3.3 The prostaglandin

Early experience was with the prostaglandins dinoprostone and gemeprost, which are expensive, unstable at room temperature and not provided in many New Zealand hospitals. Published trials comparing misoprostol with dinoprostone (Jain and Mishell 1994) and gemeprost (el-Refaey, Hinshaw et al. 1993; Jain and Mishell 1994; Hinshaw, el-Refaey et al. 1995; Ho, Chan et al. 1996; le Roux, Pahal et al. 2001) have shown that misoprostol is equally effective, produces fewer side effects and is cheaper and easier to use.

The New Zealand Mifegyne® data sheet does not specify the prostaglandin or the dose to be used for mid-trimester induction.

Misoprostol is not registered anywhere for obstetric or gynaecological use. Its registered use is for prevention of gastric and duodenal ulcers associated with the use of non-steroidal anti-inflammatory drugs. The manufacturer, Searle, sent a letter to American healthcare professionals in August 2000, elaborating on its data sheet warning against the use of misoprostol in pregnant women.

Goldberg et al. (Goldberg, Greenberg et al. 2001) in the NEJM January 2001, reviewed the obstetric uses of misoprostol and concluded "*misoprostol is one of the most important medications in obstetrical practice... The non experimental, off-label*

use of a drug requires sound scientific evidence.” The article summarises the “*strong and consistent evidence*” to support the use of misoprostol for induction of labour in the second and third trimesters as well as its use in first trimester abortion, listing 95 references. An editorial in the same issue (Hale and Zinberg 2001) followed by a letter from the manufacturer (Friedman 2001) continued the debate. Friedman stated “*we fully support the role of physicians, using their professional judgement, to prescribe an approved pharmaceutical product for a use outside of its FDA-approved indication in the best interest of their patients, on the basis of published research, expert clinical opinion, or their own clinical experience.*”

Because misoprostol is not registered for use in abortion, patients must sign an informed consent, which states that the drug is not registered for this purpose, and that the use is evidence-based.

Earlier licensed protocols all used oral prostaglandins. Some published studies suggest that the use of vaginal misoprostol shortens the induction-abortion interval and lowers the total dose of prostaglandin required (Ho, Ngai et al. 1997; Wong, Ngai et al. 2000). Templeton’s Unit in Aberdeen published their comparison of regimes using vaginal misoprostol with regimes using a combination of vaginal and oral misoprostol, which showed no significant difference (el-Refaey and Templeton 1995). Others have tried different regimens of vaginal dosing (Wong, Ngai et al. 2000).

3.4 Interval between mifepristone and the prostaglandin

The Mifegyne® data sheet recommendation is for a 36-48 hour interval. Published trials that suggest that this interval may be shortened without significantly altering the outcome have been done only in the first trimester (see 4.3.2). We are not aware of any trials showing the impact of altering this interval in second trimester patients. Some units which are familiar with offering prostaglandin-only inductions may initially find it difficult to ask the women to wait between the drugs. However most units find that this time spent in preparing for the induction process can be beneficial for the women, and any extra anxiety is outweighed by the very significant benefits of a shortened procedure on the second day.

3.5 Second trimester protocols

Protocols have been developed by Level J Unit in Wellington, National Women’s and Middlemore Hospitals in Auckland, Christchurch Women’s Hospital and Queen Mary Hospital in Dunedin.

There is some variation in these protocols. Most are providing abortion mainly for fetal anomaly. Any of the units may be contacted for advice.

4. First Trimester Medical Abortion

4.1 Background

Medical abortion is a safe, effective, acceptable method of termination for pregnancies in the first trimester.

Medical abortion has been recommended by the Royal College of Obstetricians and Gynaecologists (RCOG) in the United Kingdom as the method of choice for women with pregnancies of 49 days or less and as an appropriate method for women in the 7-9 week gestational band (RCOG 2000).

Medical abortion presents several advantages over a surgical procedure:

- There is no risk of trauma to the cervix or uterus, such as perforation.
- There is no anaesthetic risk.
- It is non-invasive and therefore the risk of infection is less.
- Its safety does not depend upon operator skills.
- Many women perceive it to be more natural, less invasive, private and more under their control.

In many countries half of abortions within approved gestational limits are performed using mifepristone, e.g. in France (56%), Scotland (61%) and Sweden (51%) (Jones and Henshaw 2002), although the rate is much less in England.

4.2 Gestational age

4.2.1 Registered use

Mifegyne® is approved under Section 21 of the Medicines Act 1981 for use as a medical alternative to surgical termination of intra-uterine pregnancy. There is no specified limit to the stage of pregnancy at which this method can be used.

The Mifegyne® data sheet (see Appendix 1), which supports this usage, recommends the following dosage and administration:

“As a medical alternative to surgical termination of intra-uterine pregnancy in early pregnancy: 600 mg mifepristone (3 tablets) in a single oral dose followed 36-48 hrs later, by the administration of a prostaglandin analogue; misoprostol 400 mcg orally (up to 49 days) or gemeprost 1 mg vaginally (up to 63 days).”

4.2.2 49-63 days' gestation

As detailed below (4.3.3) recently published evidence supports the effectiveness and safety of misoprostol as an alternative to gemeprost at a later gestational age of pregnancy as well up to 49 days. Ashok et al. (Ashok, Templeton et al. 2002), with a large series of over 4000 patients, demonstrated the safety and effectiveness of medical termination up to 63 days of pregnancy.

With most published regimes the greater the gestation, the more reported risk there is of failure and of complications (McKinley, Thong et al. 1993; Ashok, Penney et al. 1998). More recently, however, Ashok et al., in their review of over 4000 medical abortions up to 63 days' gestation (Ashok, Templeton et al. 2002) using a second dose of misoprostol after 4 hours if abortion does not appear imminent, show no significant difference in outcome between <49 and <63 days.

4.2.3 9-13 weeks' gestation

Other published experience demonstrates the safety of medical termination with mifepristone during the 9 to 13 week period (Ashok, Flett et al. 1998; Carbonell Esteve, Varela et al. 1998; Carbonell, Varela et al. 1999; Ashok, Kidd et al. 2002; Hamoda, Ashok et al. 2003).

4.2.4 Early pregnancy with no visualised sac

How early in pregnancy can medical abortion be safely performed? When ultrasonography is performed in very early pregnancy, the findings are not always conclusive in both identifying an intrauterine gestation and excluding an ectopic pregnancy. Transvaginal probe is essential to identify a sac in very early pregnancy.

There is no general agreement about management of early medical termination before the sac is visualised. Fjerstad and Creinin (Fjerstad and Creinin 2003) have discussed the relevant issues. Schaff (Schaff, Fielding et al. 2001) published a series of 30 early medical abortions when no sac was present. Many users still prefer to delay the termination until a sac can be visualised, to exclude the presence of an ectopic pregnancy.

Correlation with serum β hCG is useful. Women with levels >2000 IU/L for vaginal probe or >3600 IU/L for abdominal probe but no sac demonstrated should be investigated for ectopic pregnancy.

4.2.5 Summary

In clinically controlled circumstances medical abortion remains an alternative to surgical abortion at any gestational age. Beyond 63 days of pregnancy, present knowledge indicates that women should remain in a clinic or hospital until the termination is completed, as there is no published clinical experience to support safety of termination at home.

4.3 The method

The New Zealand data sheet (Appendix 1) recommends Mifegyne® 600 mg followed 36-48 hours later by misoprostol 400 mcg orally (up to 49 days) or gemeprost 1 mg vaginally (up to 63 days).

Peer reviewed published literature includes a range of other protocols with varying doses and, for misoprostol, route of administration.

4.3.1 Mifepristone dosage

Studies using 200 mg of mifepristone instead of 600 mg show no statistical difference in efficacy between the two doses (McKinley, Thong et al. 1993; 1999; Schaff, Eisinger et al. 1999; 2000). This is the dose recommended by the RCOG in their evidence-based guideline (RCOG 2000).

It is possible that this dose will be able to be lowered further. Creinin et al. (Creinin, Pymar et al. 2001) used 100 mg with results as good as 200 mg.

4.3.2 Interval between mifepristone and misoprostol

The approved protocol is for an interval of 36-48 hours between the mifepristone and the prostaglandin. More recent publications have suggested that this is not essential. A randomised trial showed no difference in results when misoprostol was taken 1-3 days after mifepristone (Schaff, Fielding et al. 2000; Creinin, Schwartz et al. 2001; Pymar, Creinin et al. 2001; Fox, Creinin et al. 2002).

4.3.3 The prostaglandin – misoprostol or gemeprost

The approved protocol in New Zealand recommends using misoprostol up to 49 days' gestation and gemeprost from 50-63 days' gestation (New Zealand data sheet, Appendix 1).

Gemeprost (Cervagem®) is an expensive prostaglandin, unstable at room temperature, and not provided in many New Zealand units.

Recent published experience has shown misoprostol (Cytotec®) to be safer and more effective than gemeprost at every gestation (el-Refaey, Hinshaw et al. 1993; Baird, Sukcharoen et al. 1995; Bartley, Brown et al. 2001).

The RCOG in their evidence-based guideline (RCOG 2000) state that *“Misoprostol (a prostaglandin E1 analogue) given vaginally is a cost-effective alternative for all abortion procedures for which the E1 analogue gemeprost is conventionally used (early medical abortion, cervical priming, mid-trimester abortion).”*

4.3.4 Route of administration of misoprostol

In a review article in the NEJM (Goldberg, Greenberg et al. 2001) the authors point out that only regimes of mifepristone in combination with oral (not vaginal) misoprostol have been licensed for abortion in any country. They also observe that:

“The effects of misoprostol on the reproductive tract are increased and gastrointestinal adverse effects decreased if the oral preparation of misoprostol is administered vaginally.”

Studies where direct comparisons have been made show vaginal misoprostol to be more effective than oral misoprostol and with fewer side-effects (el-Refaey, Rajasekar et al. 1995; Aubeny and Chatellier 2000; Goldberg, Greenberg et al. 2001; von Hertzen, Honkanen et al. 2003).

4.3.5 Dose of misoprostol

Recent studies using 800 µg administered vaginally have shown results with more than 90% completion within 4 hours (el-Refaey, Rajasekar et al. 1995).

Mifepristone 200 mg followed by vaginal administration of misoprostol 800 µg is now the “evidence-based protocol” used in Planned Parenthood clinics in the USA and in many UK clinics. As this is not the approved dose, informed patient consent is required.

In their published series of over 4000 abortions Ashok et al. introduced a second dose of misoprostol 400 µg given either vaginally or orally after 4-5 hours if abortion is not imminent. This increases the effectiveness, particularly in pregnancies of 50-63 days (Ashok, Templeton et al. 2002). A very recent WHO study (von Hertzen, Honkanen et al. 2003) comparing various regimes of misoprostol showed a similar increased effectiveness in gestations of 57-63 days when 800 µg of vaginal misoprostol is followed by 400 µg p.o. bid for 7 days.

4.3.6 Informed consent

Patient consent is required to adhere to the Istar-Exelgyn agreement (see Appendix 2). For any variations from the Mifegyne® or Cytotec® data sheets, further consent specific for the variations must be obtained. Patient information should clearly explain that the variations are evidence-based and the evidence must be available for patients

to consult if they wish. Appendix 3 contains sample consent forms containing these modifications.

4.4 Management in clinic or at home

New Zealand law requires women to be in the licensed institution for the administration of both abortifacient drugs. However the choice as to whether the women remain in the clinic, and for how long, will have to be made by the individual clinic and clinician. Where possible, they will involve the woman in this decision, depending on her circumstances.

4.4.1 After mifepristone administration

After administration of mifepristone women need remain in the clinic for only a short period of time, to ensure the dose is not vomited and the patient is clinically stable. If the dose is vomited another can be given (a wait of 30-60 minutes is suggested).

4.4.2 After misoprostol administration

There is now a large volume of international experience with early medical termination:

- In the USA the vast majority of women self-administer the prostaglandin (misoprostol 800 mcg vaginally) at home.
- Some UK clinics, such as British Pregnancy Advisory Service (BPAS), have now completed a trial of allowing women to go home immediately after the administration of misoprostol. The data from this trial have not been published but are available from the authors on request if used to inform clinics on developing appropriate practice.
- In most UK clinics women are encouraged to stay on the premises 4-6 hours after misoprostol is administered. The vast majority of these women will complete the termination in that time. El Refaey et al. found 99% completed their abortions within 4 hours (el-Refaey and Templeton 1994). Those who do not may go home and will require follow-up to ensure completion.
- The Level J Unit, Wellington, audited its first year of use under the restrictive interpretation of the New Zealand law that required abortion to be completed before patients were allowed to go home. Of 65 patients: one aborted after mifepristone; 64 were given misoprostol; 60 of 64 successfully completed on the ward in less than 8 hours; 4 of 64 were given suction curettage after 8 hours; of those 4 none had visible products (in 3 histology confirmed chorionic villi) but none had any post-discharge problems.

4.4.3 Assessment of patients for early discharge after misoprostol

Fully informed patient choice must be the most important factor.

Emergency specialist services must be available (within two hours' travelling time).

The women need to have:

- access to a telephone (not toll-barred) to be able to contact the clinic/after-care services
- reliable transport or money for taxis to attend emergency services if there are complications
- access to toilet, shower/bath, laundry facilities
- support at home

First Trimester Medical Abortion

- the ability to cope independently both with pain and with bleeding
- written information about the process and the drugs used
- preparation for what the pregnancy tissue may look like
- the ability to identify problems and knowledge of how to act on them
- residence or other accommodation close to the clinic or hospital – the abortion process may take place 30-60 minutes after administration of misoprostol
- either the ability to communicate clearly in English or a support person who will remain with her who speaks good English, or the clinic can provide staff who speak the language of the patient.

4.4.4 Clinic ability to support patient at home

24-hour on-call patient advice is essential for management of medical abortion both in the interval between the administration of mifepristone and misoprostol and for any patients who are discharged home after misoprostol without having passed the products of conception. This support must be given by staff who are experienced and informed about management of medical abortion and who can talk the woman through the process if she is distressed by the amount of pain and bleeding which normally accompanies early medical abortion as well as advise on management of any serious complications.

Some clinics have expressed concern that providing on-call patient advice will not be possible within their service and this will prevent them offering early medical abortion to their patients. Given the small population of New Zealand a cost-effective way to overcome this problem could be easily devised by cooperation between clinics providing early medical termination of pregnancy.

The British Pregnancy Advisory Service and Marie Stopes International each run a national emergency number for after-hours calls for the whole of their UK services.

4.5 Medical follow-up after first trimester medical abortion

4.5.1 Evidence

While the combination of mifepristone and misoprostol is a very good method for the termination of pregnancy, agreement on the best method of evaluating its outcome and follow-up protocols is still in its infancy. Several recent papers are beginning to evaluate the best outcome measures (Creinin 1996; Paul, Schaff et al. 2000; Creinin, Meyn et al. 2001; Harwood, Meckstroth et al. 2001; Walker, Schaff et al. 2001; Fiala, Safar et al. 2003). Some consensus recommendations are reported below.

Sequential serum β hCG measurements have been evaluated in small studies. These measurements are the best method available currently for evaluating the completion of medical termination at follow-up. If the levels are static or rising, they must be used in conjunction with transvaginal ultrasound scan (USS) follow-up of the endometrial thickness (diameter of retained products of conception) measurements. USS on its own is less reliable than β hCG measurement, especially with very early pregnancy.

4.5.2 Recommendations for follow-up

The following recommendations are made for the appropriate follow-up of women who have undergone medical abortion:

A) For women where the sac has clearly been identified as having been passed on site after medical termination of pregnancy:

- Women should have a clear understanding of how to recognise complications such as bleeding or infection and how and where to access help.
- A return visit to the clinic or to their referring doctor is recommended at 10-14 days after misoprostol administration.
- The visit should include an assessment of symptomatology and full pelvic examination where indicated.

B) For women where the sac has not been clearly identified as having been passed at medical termination of pregnancy on site:

- Women should have a clear understanding of how to recognise complications such as bleeding or infection and how and where to access help.
- The woman must at discharge be given clear instructions, both in writing and verbally, on the time, date and place of the follow-up appointment that she will attend.
- A return visit to the clinic or to the referring doctor is mandatory at 10-14 days.
- There must be clear communication between clinic staff and the follow-up doctor about arrangements for serum β hCG tests. A laboratory request form should be given to the woman, with written and verbal instructions that she is to have the blood taken 2 days before her follow-up appointment. The request form should specify that the laboratory is to send copies of the result to both the follow-up doctor and the TOP clinic.
- The follow-up visit should include full evaluation of the history, symptomatology and a pelvic examination where indicated. Confirmation is needed that the pregnancy has been terminated and that there are no complications.

4.5.3 Use of β hCG and USS for follow-up

The following are the recommended protocols for serum β hCG and USS follow-up of women who have undergone medical termination of pregnancy and have not had documented evidence of passage of sac:

- Blood for a base-line serum β hCG measurement can be taken before discharge from the clinic, with a copy to the follow-up doctor.
- Serum β hCG levels, at two weeks after early termination of pregnancy, of less than 80 i.u. indicate completion of the TOP [or <20% of the base-line value (Fiala, Safar et al. 2003)].
- If levels are higher than this at 2 weeks repeat in 72 hours; if the levels drop at a second measurement then surgical evacuation is not required.
- If level is static or rising then arrange transvaginal USS.
- If USS shows viable intrauterine pregnancy then refer for surgical termination.
- If USS shows a sac still present (but no cardiac activity) and the patient has no heavy bleeding, a second dose of misoprostol may be given (refer back to TOP clinic), or the patient may be given the option of waiting until 6 weeks post-abortion to pass the sac on her own.

First Trimester Medical Abortion

- If the patient is having prolonged heavy bleeding referral for surgical termination of pregnancy may be appropriate.
- No USS for assessing retained products of conception (RPOC) at least until 2 weeks have elapsed. This minimises the rate of unnecessary surgical evacuations.
- At two weeks USS evidence of RPOC described to be of a size greater than 5 cm in diameter **and** accompanied by heavy vaginal bleeding requires surgical evacuation.

At any stage in the process if the woman requests referral for surgical abortion, then this should be done.

4.5.4 Follow-up of women who fail to attend appointments

If completion of the abortion has not been confirmed in the clinic, there should be close communication between the referring doctor and the TOP clinic to ensure the follow-up takes place. Women will have signed a consent form agreeing to this follow-up appointment. If the woman does not attend then there must be agreement as to who takes responsibility for making contact with her.

The minimum effort that should be made is a telephone call followed by a letter to a safe address confirmed with the woman in advance (or the letter avoids any mention of the abortion). These should be carefully documented. There will be some women who do not attend despite the best attempts by providers.

4.5.5 Specialist follow-up of complications of medical abortion

In the US and UK most units provide their own follow-up and many have on-site ultrasound facilities and specialist management of complications. Most abortion units report that as their experience of medical abortion increases the need for surgical interference is reduced.

In New Zealand specialist management of complications will usually be by gynaecologists whose experience of early medical abortion is minimal. Information and education of gynaecologists in New Zealand on management of complications of medical abortion would minimise unnecessary surgery.

4.6 Patient acceptability

All regimes report high rates of patient satisfaction (1998; Winikoff, Ellertson et al. 1998; Clark, Ellertson et al. 2000; Elul, Pearlman et al. 2000; Jensen, Harvey et al. 2000; Rosing and Archbald 2000). Poenariu prepared a review for the 12th postgraduate course in reproductive medicine and biology, Geneva, Switzerland, which is available off the Internet. This review summarises the conclusions drawn and recommendations made by previous research (Poenariu 2003) including the papers mentioned above, but in particular those which give comparisons between surgical and medical abortion.

Clark et al. (Clark, Ellertson et al. 2000) reviewed the data on American women from the large multi-centre study of 2121 women in diverse sociodemographic backgrounds. They showed that women from a wide array of backgrounds found medical abortion highly acceptable, but that they choose and prefer it for different reasons. In this trial even those women who had failures appeared to be almost universally supportive of this method and no group or type of women found it largely unacceptable. Winikoff et al. showed similar acceptability of medical abortion in different cultures (Winikoff, Sivin et al. 1997).

There is a need for New Zealand research, to determine if local women also find that the method is acceptable.

4.7 Management of pain

Pain remains a decisive factor for women in the decision making process of abortion. Pain management should be based on the principles of general pain management, which can involve relatively simple and non-expensive interventions, both medical and non-medical.

Studies show pain is less severe with abortions at earlier gestations, at less than 50 days compared with 50-63 days (Spitz, Bardin et al. 1998). So every effort should be made to ensure early diagnosis and referral, with no waiting lists for medical abortion.

Christian Fiala, MPH Programme Director Reproductive Health for the Population Council, USA, reported on pain management at the British Pregnancy Advisory Service International Symposium on Abortion Care in 2001 (Fiala 2001).

Women report less pain when the choice of early medical abortion has been their own decision, and when they have accurate information before the procedure and high quality care throughout. Women who receive a description of the sensations accompanying a procedure have less distress than do those informed only of the procedure itself (Johnson 1973).

Parity has a significant influence on pain (Westhoff, Dasmahapatra et al. 2000; Suhonen, Heikinheimo et al. 2003) with primiparous women requiring significantly more analgesia. Westhoff et al. found the use of narcotic analgesia (codeine) more prevalent in women undergoing medical abortion at home than in women in a clinic setting, but the most important determinant of narcotic was clinic providing care. Use of narcotic analgesia was less prevalent among Asian women and among women with a gestational age of 56 days or less (Westhoff, Dasmahapatra et al. 2000).

4.7.1 Non-medical pain management strategies

- Different women feel secure in different environments. Some women prefer the security of a hospital environment; others prefer the comfort and privacy of their own home.
- Women need to know what to expect in terms of pain, bleeding and other symptoms. Information given needs to be realistic and matter-of-fact, with an implicit expectation that the women will be able to manage (Murphy, Jordan et al. 2000).
- Bed versus couch – there is no clinical need for women to be in bed and some women are more comfortable if they are in a sitting-room environment (White 1996; Fiala 2001).
- Separate room versus being together with other patients: some women prefer to be in the company of others undergoing the same experience. This can be achieved by making available a sitting-room with comfortable seating in addition to single recovery rooms.
- Emotional support is a significant factor in pain management (White 1996; Albers 1998). Nurses/midwives have a role in this (Albers 1998).
- Presence of a partner or support person – preference varies but most women would find it difficult for privacy, dignity and confidentiality not to have a private room if support people or other women were present.

- Simple care – a hot water bottle can be a most effective analgesic as can back-rubs, hot/cold packs to the lower abdomen, standing in a shower.

4.7.2 Analgesia

Non-steroidal anti-inflammatory drugs (NSAIDs):

- The Mifegyne® data sheet states: “*A decrease of the efficacy of the prostaglandin can theoretically occur due to the antiprostaglandin properties of non-steroidal anti-inflammatory drugs NSAIDs.*”
- More recent studies do not support this concern (Creinin and Shulman 1997). Ivy et al. (Ivy, Grace et al. 2003) in a double blind randomised control study showed no antiprostaglandin effect on cervical ripening but also no reduction in pain of surgical TOP.
- Current opinion is that there is no evidence that NSAIDs affect the efficacy of medical abortion with mifepristone/prostaglandin and there are some good arguments for their use. Kruse et al. (Kruse, Poppema et al. 2000) state “*NSAIDs such as ibuprofen are not contraindicated and their use does not decrease the likelihood of abortion after prostaglandin analog administration.*”
- The issue was further discussed at the International Symposium on Abortion Care organised by British Pregnancy Advisory Service, London, in 2001 (Fiala 2001) and concluded “*Since NSAIDs inhibit new endogenous prostaglandin synthesis they should have no adverse effect on exogenous prostaglandins.*”

Analgesia during medical abortion can be based on the following plan:

- Paracetamol is effective as first line treatment.
- An alternative is a NSAID such as naproxen sodium, ibuprofen or diclofenac.
- If further medication is needed codeine phosphate or tramadol can be used.
- In the in-patient setting there is the option to use a parenteral narcotic such as pethidine or fentanyl.

Some units give either paracetamol with or without codeine, or a NSAID at the same time as or before the misoprostol as prophylaxis.

Analgesia is more effective if given before the pain becomes distressing (Fiala 2001).

4.8 Back-up medical services

Early medical abortion can be provided in freestanding licensed abortion clinics. The need for easy access to emergency specialist gynaecological services for the management of complications is no different from that currently needed for surgical abortion. However the specialist services will usually not be familiar with managing the complications of medical abortion, which are not the same management procedures as those needed after surgical abortion.

Before offering early medical abortion clinics should have discussions with their local specialist services to ensure that back-up will be provided and to set in place clear guidelines on how, when and where the specialist facility can be accessed.

Combined training with the abortion clinic, referring doctors and specialist services on management of complications of abortion as well as a process for review of complications, would improve outcomes for women.

5. Drugs – Actions, Interactions and Contraindications

5.1 Drug names

Cytotec®, misoprostol

Mifegyne®, mifepristone (RU 486)

5.2 Drug actions

Mifepristone is a synthetic steroid derived from 19-nor-testosterone. It is a selective progesterone receptor modulator (SPRM). It has an antiprogesterone effect produced by blocking progesterone receptors (Leonhardt and Edwards 2002). It also binds to the glucocorticoid receptors but not to the mineralocorticoid receptors.

Misoprostol is a synthetic prostaglandin E analogue which has a direct effect on the uterus and cervix, causing uterine contractions and cervical dilatation.

5.3 Presentation and storage

Mifegyne® (mifepristone) is presented as a 200-milligram tablet and Cytotec® (misoprostol) as a 200-microgram tablet. Both are stored at room temperature.

5.4 Cost of the drugs

Mifegyne® costs \$180 for packets of 3 x 200 mg tablets.

Cytotec® costs 47 cents per 200 mcg tablet.

5.5 Contraindications to mifepristone / prostaglandin abortion

See Mifegyne® data sheet, Appendix 1.

5.5.1 Absolute contraindications

- Known hypersensitivity to prostaglandins, mifepristone or any component of the product
- IUCD in situ after failure to remove
- Chronic adrenal failure
- Severe asthma uncontrolled by corticosteroid therapy
- Porphyrias

5.5.2 Relative contraindications

- Corticosteroids – long term or current treatment
- For patients with asthma who use inhaled corticosteroid therapy it is recommended that the dose be doubled during the 48 hours preceding the administration of mifepristone and continued for about one week
- Cardiovascular disease (angina, Raynaud's disease, cardiac arrhythmias, cardiac failure, severe hypertension)
- Bleeding disorders
- Multiple uterine scars or history of uterine rupture – this is a high risk situation and women should be fully informed about the risks. Specialist consultation is recommended and a plan for careful maternal monitoring.

Drugs – Actions, Interactions and Contraindications

- Women over 35 who smoke more than 10 cigarettes a day
- In the absence of specific studies:
 - Breast feeding – mifepristone theoretically may be excreted in the milk. (It may consequently be advisable to recommend women to stop breast-feeding for up to one week and to advise how to maintain milk supply by expressing)
 - Renal failure, liver failure or malnutrition.

5.6 Side effects

5.6.1 After mifepristone administration

Women who have smoked until just before the administration of this drug may sometimes show some degree of “asthma” type symptoms due to bronchoconstriction. This may be relieved by the use of beta agonist inhalers.

Women who vomit copiously within an hour of receiving the drug may not show its full action as it may be brought up within the vomitus. (A second tablet of mifepristone should be given if there is any doubt.)

More than 50% of patients will have some bleeding in the 48 hours after administration of mifepristone and 2-5% of women will complete their abortion in this time.

Teratogenicity: The Mifegyne® data sheet states “*Patients must be informed that in the event of failure and a continuing pregnancy the foetus may be exposed to a risk of malformation.*” The risk of malformation has not been clearly shown and if present is significantly lower than that with misoprostol (Pons, Imbert et al. 1991; Pons and Papiernik 1991; Sitruk-Ware, Davey et al. 1998).

5.6.2 After misoprostol administration

- Women will usually experience uterine contractions or cramping (10-45%) in the hours following prostaglandin intake.
- Nausea, vomiting, and diarrhoea are very common after misoprostol but may be controlled with appropriate medication.
- All women will experience some bleeding. The amount increases with gestational age. Heavy bleeding occurs in about 5% of cases and from 0 – 4% may require curettage of the uterus for haemostasis.
- Uncommonly, hypotension (0.25%)
- Uncommonly, skin rashes (0.2%). Single cases of urticaria, erythroderma, erythema nodosum and epidermal necrolysis have been reported.
- Vagal symptoms are common (hot flushes, dizziness, chills). Fever is uncommon.
- Rare cases of headaches and of malaise have been reported.
- Misoprostol is known to be teratogenic in the first trimester. Mobius’ syndrome (congenital facial paralysis) and limb defects have occurred in the infants of women who have taken misoprostol during the first trimester in unsuccessful attempts to induce abortion (Gonzalez, Vargas et al. 1993; Pastuszak, Schuler et al. 1998; Sitruk-Ware, Davey et al. 1998). In a more recent study (Orioli and Castilla 2000) of infants exposed to misoprostol in utero a number of congenital

malformations but not Mobius' syndrome were noted. Goldberg in her review article on misoprostol (Goldberg, Greenberg et al. 2001) reviews the literature on congenital malformations in infants exposed to misoprostol.

6. Model Process for First Trimester Medical Abortions

This process is based on that developed and used in the Level J Unit, Wellington Hospital. The roles are those used by that clinic and may be variously interchanged between appropriately qualified staff.

This model process deals with clinical procedures. The legal requirements must be met before the clinical process is applied but are not referred to in this document.

6.1 Patient referral

The referring doctor should counsel the patient about the option of medical abortion for early pregnancies – see Client profile below.

The doctor should provide written patient information on medical abortion options (for sample see Appendix 6).

All usual clinic referral requirements should be fulfilled. This includes full medical history, exclusion of ectopic pregnancy, infection screen and antenatal bloods.

The referring doctor must accurately assess the gestation by history and clinical assessment including routine ultrasound assessment. Transvaginal ultrasonography should be requested but should be delayed until 35 days amenorrhoea or serum β hCG >2000.

If the patient is considering medical abortion, she should receive a clinic appointment as soon as possible to ensure the medical abortion can be given before 63 days or according to the clinic protocol.

6.2 Client profile

- Women with pregnancy <9 weeks (63 days) amenorrhoea at time of mifepristone dose
- Intra-uterine pregnancy confirmed by U/S scan
- There are no medical contraindications (see 5.5 above)
- Social contraindications:
 - Indecision about having an abortion
 - Unwillingness to have a surgical abortion if medical abortion fails
 - Lack of direct telephone access, e.g. phone not toll-barred if the woman lives away from the clinic area
 - Is unable to cope with the likely pain and bleeding or lacks the support she would need
 - Does not have the ability to identify problems and know how to act on them
 - Transport problems (for return visits and in the event of an emergency)
 - Inability to communicate on telephone or to have support person who speaks English
 - Lives more than two hours' travelling time from the clinic or hospital.

6.3 First clinic visit – Day 1

6.3.1 Counselling

(For more detail on counselling, see also Section 9, Counselling for Medical Abortion.)

- Options-counselling as per usual. This may be done at an outreach clinic.
- If women fit the client profile for medical abortion discuss medical abortion as an alternative to surgical abortion.
- Discuss the advantages of early medical abortion. For example, medical abortion is non-invasive, it avoids surgical and anaesthetic risk and can occur very early in pregnancy, it has been perceived by many patients to be more natural, and it allows more privacy and control. Give information about the advantages of early surgical abortion.
- Review adverse effects: bleeding and cramping (usually heavier than with menses) are to be expected; diarrhoea and other gastrointestinal side effects are common; there is a longer duration of bleeding than after surgical abortion; there is a very small risk of prolonged or heavy bleeding requiring a vacuum aspiration surgical procedure. (The adverse effects can be discussed more fully with the medical or nursing staff, as will be the instructions on what to do in an emergency.)
- Explain to the patient the three-visit procedure (mifepristone, misoprostol and follow-up to ensure completion) and the need to adhere to the protocol. If the abortion is unsuccessful, a surgical abortion must be performed due to the possible teratogenicity of misoprostol. Ensure that she agrees and is able to return for the three-visit procedure.
- Ensure that the woman is clear about her decision to have an abortion and fits the client profile (see 6.2).
- Give information about the process and the drugs used.
- Offer culturally appropriate assistance, e.g. a Maori health unit, and the provision of an interpreter if necessary.
- Discuss contraceptive options and give information.

6.3.2 Medical assessment

(This may be done by one doctor, if first certification has already been provided, or, as in Level J Unit, divided between two certifying doctors.)

- Check information provided by referring doctor and results of all tests performed.
- Obtain a medical history and check adequate dating of the pregnancy.
- Bimanual examination is advised to exclude adnexal pathology.
- Review of ultrasound examination results is recommended to assess any possibility of ectopic pregnancy. Ultrasound examination cannot completely exclude the presence of an ectopic pregnancy and if there are clinical grounds for suspecting ectopic pregnancy, serum β hCG estimations should be performed. (Identification of intrauterine sac can be expected on transvaginal ultrasonography with β hCG >2000.)
- Rule out contraindications to medical abortion – see 5.5 Medical contraindications and 6.2 Client profile.
- Ensure treatment of any infection.

Model Process for First Trimester Medical Abortions

- Review plans for post-abortion contraception:
 - Patients who choose oral contraceptives may take the first pill the day after the completion of their abortion
 - Depo Provera can be given after completion of the abortion
 - Patients may begin to have sexual intercourse with barrier contraception when they have stopped bleeding
 - Patients who choose sterilisation should be referred as appropriate to avoid delays, and interim contraception should be put in place
 - IUCD may be inserted one week after proven completion of the termination.
- Review the patient consent form, which takes into account the Istar-Exelgyn agreement as well as evidence-based changes in the protocol for mifepristone and misoprostol and consent for Anti-D if indicated. The patient is to sign and date the form and the medical assessor is to sign as witness (see 4.3.6 and Appendix 3 for sample consent).
- Prescribe:
 - Anti-D if indicated
 - Mifepristone 200 mg p.o., misoprostol 800 mcg p.v. initial dose and a second dose of 400 mcg after 4 hours if delivery of products not imminent.
 - Pain relief and anti-emetics for Day 2.

6.3.3 Nurse/midwife care

Some of the above assessment may be carried out by a nurse/midwife. In particular, the patient may feel more comfortable when the nurse gives information on what to expect in the way of pain and bleeding, provides education on what is regarded as normal, and discusses practical details such as use of pads/tampons/bedpans and when to ring the emergency number. The patient should be given written information on how to call that number.

6.3.4 Administration of the treatment

- Administer Anti-D if indicated.
- Administer mifepristone 200 mg tablet by mouth. Keep patient under medical/nursing observation for one hour to ensure there is no reaction to the drug and that it has been ingested. (Legal requirement – mifepristone must be administered under the responsibility and control of the prescribing doctor, in the presence of the doctor or a health professional, and on the licensed premises.)
- Give the patient written instructions.

6.3.5 Support for patient at home during interval between mifepristone and misoprostol

- Make sure the patient knows how to reach provider on-call. The patient information sheet should include instructions about how to call or page the provider, and the information should be reviewed to be sure she understands.
- If the patient experiences significant pain or bleeding she may need earlier admission. 50% will experience some bleeding and 2-5% of patients will complete the abortion within 48 hours after the mifepristone.

- On-call provider(s) should use triage assessment guides (see Appendix 4 for sample) and be clear about when and where to refer any problems

6.4 Second clinic visit – Day 2

In the normal course of events, if no symptoms have caused the client to come in early, she will be re-admitted to the clinic in the morning 36-48 hours following mifepristone administration. (Legal requirement – misoprostol must be administered under the responsibility and control of the prescribing doctor, in the presence of the doctor or a health professional, and on the licensed premises.)

6.4.1 Discharge home immediately after misoprostol administration

Ensure the woman has information about what to expect, supplies of analgesia which may be needed, and information on when and how to obtain assistance.

These patients will need a 24-hour telephone number to contact for advice on management of pain, bleeding and any unexpected side effects. The health professional must be familiar with management of early medical abortion and have clear written protocols to follow in giving advice. Language may be a problem. Back-up access to emergency gynaecological services must be available if problems occur and the patient requires admission.

6.4.2 Patient remaining in clinic after misoprostol administration

Management of the patient for the second day can be done entirely by an experienced nurse/midwife who will:

- Ensure that all administrative procedures are complete
- Take temperature, pulse and blood pressure base-line recordings then hourly until delivery
- Perform vaginal examination and insert misoprostol 800 mcg into the posterior vaginal fornix
- Make the client comfortable and await events.

Over the next 4-6 hours the nurse/midwife will:

- Inspect all body fluids passed for products of conception (use disposable bedpans)
- Administer comfort measures and analgesia as required by patient
- Offer a regular diet until contractions commence then fluids only.

Once products have been passed, the client is rested, given a light diet and discharged home.

The woman must be given clear instructions on how and who to contact for advice on post-abortion complications and access to emergency gynaecological services in the event of severe complications after discharge.

6.4.3 Analgesia

Encourage non-pharmaceutical pain management strategies (see Section 4.7).

Offer simple analgesia and/or anti-emetic routinely before the misoprostol insertion and repeat as required.

Medications will need to have been charted by a doctor according to clinic protocol (see Section 4.7 for discussion of options).

6.4.4 Possible complications

Fever: Temp >38°C for >1 hour – arrange blood culture and give antibiotic therapy.

Haemorrhage: Medical assessment if more than 2 maxipads per hour for 2 hours.

Post-abortion bleeding: This may go on for much longer than with surgical TOP but if the patient is soaking a pad per hour for more than 10-12 hours or exhibiting signs or symptoms of hypovolaemia, medical assessment is needed.

Allergic reaction to any of the medications.

6.4.5 Failure to complete under clinic observation

Clinics may choose to offer support for a limited period or the patient may go home immediately after misoprostol administration (see 6.1 above)

Discharge home after 4-6 hours in the clinic:

- 5 - 10% of patients may fail to pass the conceptus within 6 hours.
- Before discharge, the doctor or nurse/midwife can perform a vaginal speculum examination to check that products are not sitting in the vagina or cervix and can easily be removed.
- The patient can be discharged to complete the termination at home. However she requires access to telephone support and advice for the management of symptoms (pain and bleeding) she is likely to experience at the time of completion of the abortion (see 4.4.3 above).
- The woman must be given clear instructions on how and who to contact for advice on post-abortion complications and access to emergency gynaecological services in the event of severe complications after discharge.

6.5 Final medical consultation to ensure abortion is complete

A further visit is mandatory in 10 – 14 days to ensure the abortion is complete and there are no complications with bleeding or infection.

The patient will have already signed consent to this taking place.

This follow-up visit can be provided by the clinic or by the referring doctor. Referring doctors will need continuing medical education and adequate information about management of patients after medical abortion.

If the referring doctor is to do the follow-up, the clinic providing the abortion should appoint a designated health professional from its staff to keep a record of each patient and ensure follow-up has taken place before the patient file is closed off. A staff member should phone the referring doctor if information is not forthcoming.

Evidence of no on-going pregnancy: see 4.5 above.

7. Premises and Facilities

7.1 In the clinic

- Abortion facilities must comply with the requirements of section 21 of the Contraception, Sterilisation, and Abortion Act 1977.
- All current licensed institutions have facilities for performing surgical abortion, although surgical procedure rooms are not needed for early medical abortion.
- There is a statutory requirement under the CS & A Act for all institutions providing abortion to have access to overnight-stay facilities (s.21(1)(a) or s.21(2)(c)). These apply irrespective of whether medical or surgical abortions are performed.
- Current published literature supports the safe and effective practice of medical abortion in diverse settings (Mackenzie and Yeo 1997; Breitbart, Rogers et al. 2000), ranging from hospital-based (Ashok, Templeton et al. 2002) and freestanding clinics (Spitz, Bardin et al. 1998; Schaff, Eisinger et al. 1999) to solo practitioners' offices (Hausknecht 1995).
- Hospitals that have an abortion licence could develop early medical abortion facilities separate from the surgical facility. For patients who remain in the clinic until the abortion for up to 8 hours, accommodation in a set-up similar to the single recovery rooms for surgical abortion is appropriate.
- Day 1 of the early medical abortion process requires similar facilities to pre-abortion assessment of surgical patients. Patients given mifepristone can remain ambulatory.
- RCOG guidelines (RCOG 2000) recommend the privacy of single rooms for all women having medical abortions for the misoprostol induction.
- It is in the interests of all women and their support people to separate women undergoing abortion – for whatever reason – from women whose pregnancies are being preserved, birthing or post-natal women, and babies.
- Facilities can be combined for spontaneous pregnancy loss and induced abortion for any reasons: emotional, physical reasons and fetal anomaly. Many UK units have such integrated services. Consumer consultation would be appropriate before any change is introduced here.
- There is an advantage in women keeping upright and active during the labour process. However after narcotic analgesia, women need to be able to lie down, and differences in pain levels and coping ability mean that some women prefer to be recumbent. Many overseas clinics manage women in a sitting-room environment.
- Access to toilets is crucial – ensuite is ideal. Disposable bedpans need to be put into toilets so that products can be viewed.
- Hot water bottles, heat pads and cold packs are first line pain relief and comfort measures.
- Housekeeping and infection control need to be managed because of the copious blood loss. Squeeze bottles with chlorine for toilets are useful.

Premises and Facilities

- Increased publicity at the time of introducing a medical abortion service may increase threats from protestors and it would be timely to review the unit's security provisions.

7.2 At home

Part of the assessment for women wanting to go home to abort after misoprostol administration is of physical facilities – access to toilet, shower/bath, and laundry facilities. Also (see 4.4.3) support, access to a telephone, transport, supplies of pain relief and pads, etc.

7.3 Ultrasound

Easy access to ultrasound scanning with vaginal probe is essential for provision of medical abortion.

It is a highly recommended part of international guidelines and clinical protocols that a transvaginal ultrasound scan (USS) is performed before an early medical termination. This ensures that an intrauterine embryonic sac with a fetal pole has been recognised. If this has not been recognised, it helps to point further management and follow-up in the right direction.

Ultrasound does not necessarily have to be performed in the unit providing the medical abortion. However, it is extremely difficult to guarantee urgent access to scanning if the service has to compete for the variable access provided in private hospitals or with the overloaded obstetric/gynaecological ultrasound scanning departments in the public hospitals. It would be wise for the large units to have their own ultrasound scanning services on site.

As well as pre-abortion routine USS, access to scanning during the procedure ensures a safe clinical service. Women who bleed heavily after mifepristone, for whom there is doubt about whether they have already aborted, may need to be re-scanned before misoprostol administration. This is not uncommon as up to 5% of the women will complete their abortions after mifepristone alone, and 50% will have some bleeding in this period.

To help determine the appropriate management, further ultrasound assessment may be needed at any stage of the procedure if pain or haemorrhage occurs.

It is essential to incorporate risk management and limitation strategies at the outset when establishing any new procedure, and easy access to ultrasound services is part of this for medical abortion.

7.4 Written materials

- Clear, accurate, user-friendly written information must be available for clients at all stages – pre-decision, pre-procedure, post-procedure (see Appendix 6 for examples of pamphlets).
- Information should be available in languages other than English to meet the needs of the client base.
- Information for referring doctors is particularly useful to enable early referral (see Appendix 7).

8. Staffing and Staff Training

Planning for the introduction of medical abortion requires a general assessment of staff levels and training. Appendix 5 is “A general guide for initiation of medical abortion services”, adapted from Breitbart, Rogers and VanDerhei, which provides a useful review of issues to be considered.

Administrators, receptionists, counsellors, nurse/midwives and medical and housekeeping staff in an abortion clinic are all involved directly or indirectly in every aspect of the medical abortion process.

8.1 Staffing levels

As only licensed clinics (for surgical procedures) can provide medical abortion, unless there is a change in the regulations, early medical abortion will usually be incorporated into existing surgical facilities. Hospitals that have an abortion licence could develop an independent early medical abortion service separately.

Clinic staffing requirements will differ only slightly from those required for surgical termination. The time required for counselling and assessment for medical abortion may be greater initially, but this should decrease as all staff become familiar with incorporating medical abortion advice into their routines. Once the decision for medical abortion is made and informed consent obtained, it is advisable that the woman remains in the clinic for up to an hour after the administration of mifepristone, but little supervision is usually required in this time unless there is vomiting or some other complication.

When the patient returns for the misoprostol administration, if the patients remain in the clinic, staff levels are similar to those required for pre-and post-operative surgical care, without the need for theatre staff.

Level J Unit, Wellington, staffs its abortion unit with approximately one nurse/midwife and one coordinator to 4 patients. This number appears appropriate for medical or peri-operative surgical patients. A small proportion of patients may require a longer time on the premises, e.g. up to 8 hours.

Staff hours required for provision of a second trimester abortion service will be significantly less than those for an induction of labour without mifepristone because of the reduced time interval between misoprostol administration and delivery.

8.2 Provider acceptability

There are few studies of provider acceptability of medical abortion. Winikoff (Winikoff 1995) reviewed some early studies that we have not been able to obtain. Marwick (Marwick 1994), in a report on nurses in Aberdeen, apparently suggested that the introduction of medical abortion to a clinic already providing surgical abortion can alter job satisfaction because of adjustments in tasks. The report suggested that providers should allow staff to redistribute their functions so that those who prefer to be more (or less) involved with medical abortion patients can seek suitable assignments. This is probably even more relevant in a service providing second trimester abortions.

8.3 Role of nurse/midwife

Staffing and Staff Training

(McKee and Adams 1994; Timpson 1996; White 1996; Mackenzie and Yeo 1997; Narrigan 1998; Murphy, Jordan et al. 2000; Williams 2000).

After medical assessment, legal certification and charting of medication are complete, the clinical care of women undergoing both early and late medical abortion is likely to be in the hands of nurses and midwives, with clear guidelines for contact points with medical staff identified in the written protocols.

- The additional responsibility that nurses and midwives may assume in the provision of medical abortion may be seen as an exciting professional development and should be appreciated and exercised by the professionals and by service providers.
- Even within a dedicated abortion service, where staff have chosen to be employed, they need to have a choice about how they are involved in abortion of *advanced* pregnancies.
- Integrated units, where women undergo abortion on all legal grounds at all gestations, staffed by nurses/midwives who are choosing to do this work, are anecdotally reported (UK/NZ) to have clear advantages in the areas of job and client satisfaction.

8.4 Staff training for medical abortion

8.4.1 Introduction

- Staff orientation and training for medical abortion should involve all the personnel in the clinic as well as the referring doctors and the agencies in which they work.
- All staff must be committed to the process of providing medical abortion.
- The level of training required depends on the actual role they fulfil, but all staff should learn the appropriate way of interacting with a patient at each stage of the procedure.
- A multi-disciplinary process is in the best interests of clients and all staff working in the area of medical abortion.
- Counselling to enable the woman to make a fully informed decision and to cope with her feelings, reactions and any social impact may be offered by different health professionals: counsellors, social workers, psychotherapists, nurse-midwives and doctors depending on the local arrangements. All health professionals who counsel women need specific training in abortion counselling. Women may need referral to professional mental health services.
- Staff development, support and debrief needs should be readily met as required or requested by staff. It is desirable to provide professional supervision for all health professionals working in the area of abortion.
- Exploration of the health professional's own value system and honesty about personal issues and beliefs that might influence client management is always advisable in abortion service provision (McKee and Adams 1994; Timpson 1996; Narrigan 1998; Williams 2000).
- Processes for audit and on-going review of the service should be introduced from the beginning.
- The assessment and management of potential complications of medical abortion should be reviewed periodically within each institution.

- Anticipating possible increased media attention at the time of establishing a medical abortion service is important and discussions may be held with communications/public relations staff.
- An on-line training program on early medical abortion is available free through the US National Abortion Federation at www.EarlyOptions.org.

8.4.2 Training for referring agencies

Referring doctors need to take responsibility for keeping up-to-date with developments in abortion provision. However clinics that introduce medical abortion services would be wise to provide best practice information for their referrers, to ensure early and appropriate referral and that the clinic's requirements for referral are met. (See Appendix 6, Pamphlets on Early Medical Abortion, and Appendix 7, Guide for Referring Agencies.)

8.4.3 Administrative staff

Administrative staff in the offices of referring practitioners and in clinics (e.g. family planning clinics) should be trained to offer timely information to women so that early medical abortion can be an option.

Administrative staff in abortion clinics need training to ensure that appointment systems are managed to enable counselling and medical assessment appointments to be offered as soon as possible after referral. Understanding the advantages of having procedures take place at the earliest possible gestation will improve staff performance in this respect.

8.4.4 Training for counsellors

Those engaged in abortion counselling need to be familiar with the requirements outlined in the Abortion Supervisory Committee's *Standards of Practice for the Provision of Counselling* publication, and should have regular supervision/peer review for their professional practice. Specific training in the process of medical abortion using mifepristone and misoprostol is advisable to familiarise health professionals providing counselling with the physiological, logistical and psychosocial aspects of the procedure.

Counsellors need to be knowledgeable about the need for all women (including those in the second trimester) to discuss their options, and to be adequately informed about the stage of development of the fetus and the procedure, their feelings and beliefs about abortion and their pregnancy, and their possible feelings following abortion.

Counsellors should recognise that women facing the choice of abortion for fetal anomaly also need access to specialised genetic counselling, and that there are particular grief issues arising from facing abortion of a wanted pregnancy.

Counselling training should also include post-abortion counselling.

Counsellors must be non-judgemental and qualified to assess the needs and the coping mechanisms of women facing abortion for any reason.

Counsellor training for early medical abortion will require familiarisation with the literature from other countries on the physical, emotional and social aspects and the consumer satisfaction evidence. Visual aids (for example laminated comparison charts) are useful to support discussion on the relative advantages and disadvantages of early medical and early surgical abortion and stages of pregnancy development.

For all counselling training requirements contact the Abortion Supervisory Committee's Regional Counselling Advisor

8.4.5 Medical staff training

Clinical leaders must ensure background literature and detailed protocols are available for all medical staff. Depending on the prior knowledge of medical staff, appropriate staff training should take place before early medical abortion is offered.

Peer review is important, particularly over the first few months when units report a “steep learning curve” for all staff.

8.4.6 Nurse/midwife training

A midwifery perspective is relevant in the care of women undergoing medical abortion – particularly mid-trimester – though care can be in the hands of adequately trained and supervised registered nurses (White 1996; Albers 1998).

Managers and nurse/midwife leaders must ensure that adequate education and regular professional supervision to enable review of practice and debrief mechanisms are readily available.

Training for nurse/midwife staff needs to incorporate physical, mental, emotional, cultural and spiritual aspects of abortion care. Also needed are basic counselling skills, including an understanding of the need for clear boundaries and mechanisms for debriefing and reviewing practice (Timpson 1996; White 1996; Mackenzie and Yeo 1997; Murphy, Jordan et al. 2000; Williams 2000). Up-to-date knowledge of contraceptive methods is essential as this forms part of every woman’s discharge plan.

On-call staff should receive training in telephone assessment and decision making to ensure support and advice are readily available to women who are at home during parts of the medical abortion process. Standard on-call assessment guides and record sheets must be used to ensure consistency in dealing with calls and clear, acute documentation of the issues.

In both UK and US clinics, routine ultrasound examination, pelvic examination and routine swabs and bloods are all performed by trained nurse/midwife staff. Training will be required in those areas delegated to nurse/midwife staff in New Zealand clinics.

Registered nurses will require training in vaginal examination to enable the administration of misoprostol by the vaginal route. This needs to include teaching women how to self-administer vaginal misoprostol.

8.4.7 Training for specialist services

Before any medical abortion services are offered, clinics must ensure the availability of specialist gynaecological services for referral of any complications.

While it is clearly not the responsibility of an abortion clinic to train specialist medical staff, it might be wise to offer clinical information, appropriate medical literature, and combined training.

8.4.8 Training for second trimester services

The gestation of the woman might have an influence on which staff are suitable and willing to care for women undergoing second trimester abortions.

Second trimester services, in particular, put significant psychological stresses on staff and this must be acknowledged and provided for.

Because women having second trimester abortion are usually significantly more emotionally stressed, training for their management must include understanding of the reasons for women requiring second trimester abortions and how to support the women through the process.

It is in the best interests of the women to have staff who are not ambivalent about their own commitment to abortion provision.

Nurse/midwife staff who provide care must be trained in the management of labour and birth and be able to inform women about after-care, including breast care (Albers 1998).

9. Counselling for Medical Abortion

9.1 General

The counsellor's role is to discuss pregnancy options, to ensure that the decision to have an abortion is informed, voluntary and non-coerced and the patient understands the possible effects on her of the decision she makes.

The decision on the abortion should be made before discussing the methods of abortion available. The decision to terminate is generally independent of the methods of abortion available, although less so at greater gestational ages.

Giving information on methods, and assisting the patient to make choices where this is possible, may be done by counsellors, nurse/midwives or doctors, depending on the arrangement in the particular clinic.

The client's choice of method of abortion is likely to be determined by medical and psychosocial factors.

The advantages and disadvantages of medical abortion need to be outlined.

The alternatives should be discussed, such as the availability and risks of early surgical abortion in early pregnancies and alternatives in late pregnancy depending on what can be offered in the particular clinic.

The importance of adherence to protocol needs to be emphasised and the possibility of effects on the fetus if the pregnancy is left to continue after the drugs have been taken. Explain to the patient the three-visit procedure (mifepristone, misoprostol and follow-up to ensure completion) and the need for consent to alternative procedures if medical abortion fails. Clarify that she would be able to return for all visits.

Both first and second trimester medical abortion should contain the standard content of pregnancy counselling as specified in the Abortion Supervisory Committee's *Standards of Practice for the Provision of Counselling*.

At times counselling and assessment may be more intensive than for surgical abortion. This is because it will involve not just a focus on the classical abortion conflicts (socio-cultural, socio-economic, internal-emotional, interpersonal, moral, ethical, religious issues, etc.). It will also, if a first trimester abortion is sought, involve the client's choice between two methods of treatment, and the information on them that she will need in order to make that decision.

Experience overseas shows that – depending on the needs of the individual woman – counselling takes less time as staff become more familiar and comfortable with offering the procedure.

9.2 Social factors

The following factors should be assessed:

- Transport. The client must have reliable transport (use of vehicle and driver) for return visits and in the event of an emergency.
- Communication. Unless there are appropriate multi-lingual staff available in the clinic or on the 24-hour telephone line, the client must have adequate English to understand instructions and be understood by telephone or have a support person always available who is able to communicate in English. Twenty-four a day direct telephone access is required. She must be able to call a mobile phone from her telephone.

- **Childcare.** The client must have pre-arranged childcare. It must cover emergency childcare needs (e.g. middle of the night) as well as at the times of scheduled appointments.
- **Confidentiality.** Some clients wish to tell no one of their abortion. However, the client ideally should have at least one appropriate, accessible person who is aware that she is undergoing this procedure and is able to provide emotional and practical support.
- **Proximity.** The client needs to live or be accommodated within an hour's drive from the clinic or emergency hospital facilities.

9.3 Support

The woman's chosen support, whether it is partner or other, needs to have a supportive view of the TOP and the emotional ability to support the woman through the process. If the clinic permits the presence of a support person, ensure that the person does not pose a threat to staff or clients. There is no contraindication for medical abortion if the woman is going to be on her own.

Practical support – the woman ideally has someone to provide transport and to stay with her overnight.

9.4 Psychological and emotional factors

The client must have the ability to cope psychologically and emotionally with the medical abortion process.

The counsellor needs to:

- Assess those issues that may affect the client's ability to manage the abortion e.g. a history of anxiety, sexual abuse and other issues. Medical abortion may be more appropriate for such people than a surgical procedure, but assessment of coping skills is needed.
- Discuss the client's comfort level regarding the process involved in medical abortion. Is she able to deal with cramps, bleeding and possibly delivering the pregnancy tissue at home?

9.5 Second trimester abortions

For second trimester pregnancy counselling there are particular issues that may need addressing:

- Reasons for late presentation, e.g. ambivalence, denial of the pregnancy
- Ambivalence may be related to lack of support, or pressure from partner or family to continue or to abort the pregnancy.
- Fetal development, fetal movement
- Viewing the fetal tissue. This is much more difficult to avoid because of the later stage of pregnancy. It may be beneficial for the client's mental health long term if she feels able to view the tissue. However it is not desirable to force this upon the client.
- Fetal anomaly issues require referral to specialist genetic counselling for future pregnancies

Counselling for Medical Abortion

- The importance of having a post mortem examination when there is fetal anomaly should be discussed. This issue should be raised by the maternal-fetal medicine consultant or obstetrician and may also be raised by the midwife, genetic counsellor and/or the health professional providing pre-decision counselling. Written as well as verbal information is ideal. Balance must be achieved between the time parents wish to spend with their fetus/baby and the clinical/system requirements for post mortem examination. Follow-up discussion of the results will generally be arranged with the consultant. It can be useful to schedule a post-abortion counselling session to be available soon after this to assist patients to process the information as well as with grieving and achieving closure.
- Level of attachment to the pregnancy
- Other life traumas or grief issues may be part of their situation. For example, late presentation for abortion may be due to the end of the relationship, the death of an important support person or some other life crisis
- Value system – moral, ethical, religious and spiritual issues
- Assessment of risk of post-abortion mental health problems is crucial and the possible impact of the decision to abort must be discussed
- Coping afterwards – level of support and coping strategies.

9.6 Other issues

Ability to commit to the medical abortion process is important. The client must commit herself to follow up if she does not deliver within the three-visit time frame. Non-delivery in the three-day time frame may create problems for her in terms of safety or confidentiality or may create other issues.

Explore the client's own pregnancy history. Previous negative experience of TOP may become a significant counselling issue, as well as part of assessment.

The client must have a contingency plan in place to ensure that she receives appropriate support and has the ability to make return visits during the medical abortion process.

Offer culturally appropriate assistance, e.g. Maori health unit, and the provision of an interpreter if necessary. Keep in mind that a client's inability to speak English may be a barrier to undergoing early medical abortion.

Discuss contraceptive options and give information.

10. Management of Fetal Tissue

Women must be realistically informed about the appearance of pregnancy tissue at different gestations.

All clinics must have a policy in place for disposal of pregnancy tissue. This will be similar to that required for surgical abortion. There are legal, cultural, spiritual, ethical, staff training and infection control issues that need to be addressed in the policy.

There is a legal requirement for notification of the birth to the Registrar of Births Deaths and Marriages if the pregnancy is over 20 weeks' gestation or the fetus is over 400 gm in weight.

Maori clients may have particular wishes regarding the fetus or placenta/whenua.

Medical and legal terminology can distress or offend women. When discussing the pregnancy products with clients, health professionals need to take the lead from the woman, who might wish to refer to her "baby" regardless of gestation.

User-friendly written and verbal information needs to be available to women from the first visit about their rights with regard to their pregnancy tissue. It should state:

- the policy of the clinic with regard to management of the tissue and any options that the clinic provides, such as paying for cremation through private funeral directors
- the method and site(s) of disposal if the woman does not wish to take home her pregnancy tissue.
- her obligations if she does choose to take home the tissue.

Staff must be aware of the policy, their responsibilities, and the need for respect and dignity in the management of pregnancy tissue. They must have sensitivity towards women and their individual beliefs and needs with regard to their pregnancy tissue.

For women who abort at home discussion is required on disposal of tissue. Many women will not see products of conception because they are small and passed along with heavy blood loss. If fetal tissue is identified women may choose to deal with it as above.

When termination has been performed for fetal anomaly it is important to attempt to provide confirmation of the fetal abnormality after delivery, preferably by post-mortem or histology. If there is not consent for post-mortem or histology, a second best option should be recommended such as ultrasound. The nursing/midwifery staff managing care during the procedure will have to know and understand the pathology requirements and be adequately prepared to discuss these sensitively and realistically with the woman and her support person(s).

Appendix 9 is the Level J Unit client information on management of pregnancy tissue.

11. Evaluation and Audit

11.1 Audit in the clinic

Each clinic should establish procedures for review of their medical abortion service. This should include procedures for assessing client satisfaction as well as reviewing how the service is working from the staff perspective.

Designated staff should maintain records of any complications and any critical incidents. These data should be analysed periodically to discover trends.

Some clinics are already accredited by outside agencies and this is to be encouraged.

The Abortion Supervisory Committee is looking at ways of collecting and analysing data on medical abortion and we can expect some outcome from this by 1 January 2005.

11.2 National audit

There is a need for New Zealand data on medical abortion. It cannot be assumed that data collected in other cultures are entirely relevant to New Zealand.

Istar Limited is offering to audit Mifegyne® use in New Zealand and would greatly appreciate clinics providing non-identifiable information about each abortion. The company is offering to collate and provide up-to-date analysis of any data that are provided.

The company can provide an Access file for information to be collected or an audit form.

11.3 Abortion Supervisory Committee

The Committee collects routine information on abortions through the ASC4 form. This form is legally required and is compulsory for providers to return. The Committee will consider appropriate modifications in line with this new service.

12. Resources

These guidelines are designed for services that wish to establish or extend the provision of medical abortion and to offer to women in New Zealand choices that have been available for many years in other parts of the world.

All papers on the reference list are available via medical libraries and are held by the Abortion Supervisory Committee.

Electronic resources are numerous and the public are already active in obtaining information about abortion via the Internet. Much of this is negative anti-abortion material that needs to be balanced by evidence-based, objective information.

Useful sites include:

www.prochoiceforum.org.uk

www.rcog.org.uk

www.earlyoptions.org

www.plannedparenthood.org

www.gynpages.com

www.cliniciansforchoice.org

New Zealand abortion providers should be encouraged to develop local websites.

References

- (1998). "Women find mifepristone safe, acceptable method." Contracept Technol Update **19**(9): 113-4.
- (1999). "Comparing the effectiveness of different doses of mifepristone." Prog Hum Reprod Res(51): 5-7.
- Albers, L. (1998). "Midwifery management of pain in labor. The CNM Data Group, 1996." J Nurse Midwifery **43**(2): 77-82.
- Ashok, P. W., G. M. Flett, et al. (1998). "Termination of pregnancy at 9-13 weeks' amenorrhoea with mifepristone and misoprostol." Lancet **352**(9127): 542-3.
- Ashok, P. W., A. Kidd, et al. (2002). "A randomized comparison of medical abortion and surgical vacuum aspiration at 10-13 weeks gestation." Hum Reprod **17**(1): 92-8.
- Ashok, P. W., G. C. Penney, et al. (1998). "An effective regimen for early medical abortion: a report of 2000 consecutive cases." Hum Reprod **13**(10): 2962-5.
- Ashok, P. W., A. Templeton, et al. (2002). "Factors affecting the outcome of early medical abortion: a review of 4132 consecutive cases." Bjog **109**(11): 1281-9.
- Aubeny, E. and G. Chatellier (2000). "A randomized comparison of mifepristone and self-administered oral or vaginal misoprostol for early abortion." Eur J Contracept Reprod Health Care **5**(3): 171-6.
- Baird, D. T., N. Sukcharoen, et al. (1995). "Randomized trial of misoprostol and cervagem in combination with a reduced dose of mifepristone for induction of abortion." Hum Reprod **10**(6): 1521-7.
- Bartley, J., A. Brown, et al. (2001). "Double-blind randomized trial of mifepristone in combination with vaginal gemeprost or misoprostol for induction of abortion up to 63 days gestation." Hum Reprod **16**(10): 2098-102.
- Breitbart, V., M. K. Rogers, et al. (2000). "Medical abortion service delivery." Am J Obstet Gynecol **183**(2 Suppl): S16-25.
- Carbonell Esteve, J. L., L. Varela, et al. (1998). "Vaginal misoprostol for late first trimester abortion." Contraception **57**(5): 329-33.
- Carbonell, J. L., L. Varela, et al. (1999). "Vaginal misoprostol for abortion at 10-13 weeks' gestation." Eur J Contracept Reprod Health Care **4**(1): 35-40.
- Clark, S., C. Ellertson, et al. (2000). "Is medical abortion acceptable to all American women: the impact of sociodemographic characteristics on the acceptability of mifepristone-misoprostol abortion." J Am Med Womens Assoc **55**(3 Suppl): 177-82.
- Creinin, M. D. (1996). "Change in serum beta-human chorionic gonadotropin after abortion with methotrexate and misoprostol." Am J Obstet Gynecol **174**(2): 776-8.
- Creinin, M. D., L. Meyn, et al. (2001). "Accuracy of serum beta-human chorionic gonadotropin cutoff values at 42 and 49 days' gestation." Am J Obstet Gynecol **185**(4): 966-9.
- Creinin, M. D., H. C. Pymar, et al. (2001). "Mifepristone 100 mg in abortion regimens." Obstet Gynecol **98**(3): 434-9.
- Creinin, M. D., J. L. Schwartz, et al. (2001). "Efficacy of mifepristone followed on the same day by misoprostol for early termination of pregnancy: report of a randomised trial." Bjog **108**(5): 469-73.
- Creinin, M. D. and T. Shulman (1997). "Effect of nonsteroidal anti-inflammatory drugs on the action of misoprostol in a regimen for early abortion." Contraception **56**(3): 165-8.

- el-Refaey, H., K. Hinshaw, et al. (1993). "The abortifacient effect of misoprostol in the second trimester. A randomized comparison with gemeprost in patients pre-treated with mifepristone (RU486)." Hum Reprod **8**(10): 1744-6.
- el-Refaey, H., D. Rajasekar, et al. (1995). "Induction of abortion with mifepristone (RU 486) and oral or vaginal misoprostol." N Engl J Med **332**(15): 983-7.
- el-Refaey, H. and A. Templeton (1994). "Early induction of abortion by a combination of oral mifepristone and misoprostol administered by the vaginal route." Contraception **49**(2): 111-4.
- el-Refaey, H. and A. Templeton (1995). "Induction of abortion in the second trimester by a combination of misoprostol and mifepristone: a randomized comparison between two misoprostol regimens." Hum Reprod **10**(2): 475-8.
- Elul, B., E. Pearlman, et al. (2000). "In-depth interviews with medical abortion clients: thoughts on the method and home administration of misoprostol." J Am Med Womens Assoc **55**(3 Suppl): 169-72.
- Fiala, C. (2001). Managing Pain in Early Medical Abortion. Abortion Care a BPAS International Symposium, London, British Pregnancy Advisory Service.
- Fiala, C., P. Safar, et al. (2003). "Verifying the effectiveness of medical abortion; ultrasound versus hCG testing." Eur J Obstet Gynecol Reprod Biol **109**(2): 190-5.
- Fjerstad, M. and M. Creinin (2003). "Sonography in Very Early Pregnancy: Providing mifepristone medical abortion when no gestational sac/no yolk sac are seen on transvaginal ultrasound." Mifematters - a publication of the Planned Parenthood/CAPS Medical Abortion Training Program Winter2003(#6): 1-12.
- Fox, M. C., M. D. Creinin, et al. (2002). "Mifepristone and vaginal misoprostol on the same day for abortion from 50 to 63 days' gestation." Contraception **66**(4): 225-9.
- Friedman, M. A. (2001). "Manufacturer's warning regarding unapproved uses of misoprostol." N Engl J Med **344**(1): 61.
- Goldberg, A. B., M. B. Greenberg, et al. (2001). "Misoprostol and pregnancy." N Engl J Med **344**(1): 38-47.
- Gonzalez, C. H., F. R. Vargas, et al. (1993). "Limb deficiency with or without Mobius sequence in seven Brazilian children associated with misoprostol use in the first trimester of pregnancy." Am J Med Genet **47**(1): 59-64.
- Hale, R. W. and S. Zinberg (2001). "Use of misoprostol in pregnancy." N Engl J Med **344**(1): 59-60.
- Hamoda, H., P. W. Ashok, et al. (2003). "Medical abortion at 64 to 91 days of gestation: a review of 483 consecutive cases." Am J Obstet Gynecol **188**(5): 1315-9.
- Harwood, B., K. R. Meckstroth, et al. (2001). "Serum beta-human chorionic gonadotropin levels and endometrial thickness after medical abortion." Contraception **63**(5): 255-6.
- Hausknecht, R. U. (1995). "Methotrexate and misoprostol to terminate early pregnancy." N Engl J Med **333**(9): 537-40.
- Hinshaw, K., H. el-Refaey, et al. (1995). "Mid-trimester termination for fetal abnormality: advantages of a new regimen using mifepristone and misoprostol." Br J Obstet Gynaecol **102**(7): 559-60.
- Ho, P. C., Y. F. Chan, et al. (1996). "Misoprostol is as effective as gemeprost in termination of second trimester pregnancy when combined with mifepristone: a randomised comparative trial." Contraception **53**(5): 281-3.

- Ho, P. C., S. W. Ngai, et al. (1997). "Vaginal misoprostol compared with oral misoprostol in termination of second-trimester pregnancy." *Obstet Gynecol* **90** (5): 735-8.
- Ivy, L. C., W. C. Grace, et al. (2003). "A study of co-treatment of nonsteroidal anti-inflammatory drugs (NSAIDs) with misoprostol for cervical priming before suction termination of first trimester pregnancy." *Contraception* **67**(2): 101-5.
- Jain, J. K. and D. R. Mishell, Jr. (1994). "A comparison of intravaginal misoprostol with prostaglandin E2 for termination of second-trimester pregnancy." *N Engl J Med* **331**(5): 290-3.
- Jensen, J. T., S. M. Harvey, et al. (2000). "Acceptability of suction curettage and mifepristone abortion in the United States: a prospective comparison study." *Am J Obstet Gynecol* **182**(6): 1292-9.
- Johnson, J. E. (1973). "Effects of accurate expectations about sensations on the sensory and distress components of pain." *J Pers Soc Psychol* **27**(2): 261-75.
- Jones, R. K. and S. K. Henshaw (2002). "Mifepristone for early medical abortion: experiences in France, Great Britain and Sweden." *Perspect Sex Reprod Health* **34**(3): 154-61.
- Kruse, B., S. Poppema, et al. (2000). "Management of side effects and complications in medical abortion." *Am J Obstet Gynecol* **183**(2 Suppl): S65-75.
- le Roux, P. A., G. S. Pahal, et al. (2001). "Second trimester termination of pregnancy for fetal anomaly or death: comparing mifepristone/misoprostol to gemeprost." *Eur J Obstet Gynecol Reprod Biol* **95**(1): 52-4.
- Leonhardt, S. A. and D. P. Edwards (2002). "Mechanism of action of progesterone antagonists." *Exp Biol Med (Maywood)* **227**(11): 969-80.
- Mackenzie, S. J. and S. Yeo (1997). "Pregnancy interruption using mifepristone (RU-486). A new choice for women in the USA." *J Nurse Midwifery* **42**(2): 86-90.
- Marwick, D. (1994). "A comparison of surgical vacuum aspiration abortion with medical abortion using mifepristone (RU486) and gemeprost: Implications for nursing staff." *British Journal of Family Planning* **20**: 8-10.
- McKee, K. and E. Adams (1994). "Nurse midwives' attitudes toward abortion performance and related procedures." *J Nurse Midwifery* **39**(5): 300-11.
- McKinley, C., K. J. Thong, et al. (1993). "The effect of dose of mifepristone and gestation on the efficacy of medical abortion with mifepristone and misoprostol." *Hum Reprod* **8**(9): 1502-5.
- Murphy, F., S. Jordan, et al. (2000). "Care of women having termination of first-trimester pregnancy." *Br J Nurs* **9**(21): 2235-41.
- Narrigan, D. (1998). "Early abortion. Update and implications for midwifery practice." *J Nurse Midwifery* **43**(6): 492-501.
- Orioli, I. M. and E. E. Castilla (2000). "Epidemiological assessment of misoprostol teratogenicity." *Bjog* **107**(4): 519-23.
- Pastuszek, A. L., L. Schuler, et al. (1998). "Use of misoprostol during pregnancy and Mobius' syndrome in infants." *N Engl J Med* **338**(26): 1881-5.
- Paul, M., E. Schaff, et al. (2000). "The roles of clinical assessment, human chorionic gonadotropin assays, and ultrasonography in medical abortion practice." *Am J Obstet Gynecol* **183**(2 Suppl): S34-43.
- Poenariu, M. (2003). Patients' satisfaction with first trimester mifepristone-misoprostol medical abortion services A literature review. Geneva, Geneva Foundation for Medical Education and Research: 15.
- Pons, J. C., M. C. Imbert, et al. (1991). "Development after exposure to mifepristone in early pregnancy." *Lancet* **338**(8769): 763.
- Pons, J. C. and E. Papiernik (1991). "Mifepristone teratogenicity." *Lancet* **338**(8778): 1332-3.

- Pymar, H. C., M. D. Creinin, et al. (2001). "Mifepristone followed on the same day by vaginal misoprostol for early abortion." *Contraception* **64**(2): 87-92.
- RCOG (2000). *The Care of Women Requesting Induced Abortion*. London, Royal College of Obstetricians and Gynaecologists: 1-9.
- Rodger, M. W. and D. T. Baird (1990). "Pretreatment with mifepristone (RU 486) reduces interval between prostaglandin administration and expulsion in second trimester abortion." *Br J Obstet Gynaecol* **97**(1): 41-5.
- Rosing, M. A. and C. D. Archbald (2000). "The knowledge, acceptability, and use of misoprostol for self-induced medical abortion in an urban US population." *J Am Med Womens Assoc* **55**(3 Suppl): 183-5.
- Schaff, E. A., S. H. Eisinger, et al. (1999). "Low-dose mifepristone 200 mg and vaginal misoprostol for abortion." *Contraception* **59**(1): 1-6.
- Schaff, E. A., S. L. Fielding, et al. (2001). "Mifepristone and misoprostol for early abortion when no gestational sac is present." *Contraception* **63**(5): 251-4.
- Schaff, E. A., S. L. Fielding, et al. (2000). "Vaginal misoprostol administered 1, 2, or 3 days after mifepristone for early medical abortion: A randomized trial." *Jama* **284**(15): 1948-53.
- Sitruk-Ware, R., A. Davey, et al. (1998). "Fetal malformation and failed medical termination of pregnancy." *Lancet* **352**(9124): 323.
- Spitz, I. M., C. W. Bardin, et al. (1998). "Early pregnancy termination with mifepristone and misoprostol in the United States." *N Engl J Med* **338**(18): 1241-7.
- Suhonen, S., O. Heikinheimo, et al. (2003). "The learning curve is rapid in medical termination of pregnancy--first-year results from the Helsinki area." *Contraception* **67**(3): 223-7.
- Timpson, J. (1996). "Abortion: the antithesis of womanhood?" *Journal of Advanced Nursing* **23**: 776-785.
- Urquhart, D. R. and A. A. Templeton (1990). "The use of mifepristone prior to prostaglandin-induced mid-trimester abortion." *Hum Reprod* **5**(7): 883-6.
- von Hertzen, H., H. Honkanen, et al. (2003). "WHO multinational study of three misoprostol regimens after mifepristone for early medical abortion. I: Efficacy." *Bjog* **110**(9): 808-18.
- Walker, K., E. Schaff, et al. (2001). "Monitoring serum chorionic gonadotropin levels after mifepristone abortion." *Contraception* **64**(5): 271-3.
- Webster, D., G. C. Penney, et al. (1996). "A comparison of 600 and 200 mg mifepristone prior to second trimester abortion with the prostaglandin misoprostol." *Br J Obstet Gynaecol* **103**(7): 706-9.
- Westhoff, C., R. Dasmahapatra, et al. (2000). "Analgesia during at-home use of misoprostol as part of a medical abortion regimen." *Contraception* **62**(6): 311-4.
- White, B. (1996). "Profession Development: Termination of Pregnancy." *Nursing Times* **92**(14,15 & 16).
- WHO (2000). "Comparison of two doses of mifepristone in combination with misoprostol for early medical abortion: a randomised trial. World Health Organisation Task Force on Post-ovulatory Methods of Fertility Regulation." *Bjog* **107**(4): 524-30.
- Williams, G. B. (2000). "Grief after elective abortion." *AWHONN Lifelines* **4**(2): 37-40.
- Winikoff, B. (1995). "Acceptability of medical abortion in early pregnancy." *Fam Plann Perspect* **27**(4): 142-8, 185.
- Winikoff, B., C. Ellertson, et al. (1998). "Acceptability and feasibility of early pregnancy termination by mifepristone-misoprostol. Results of a large

- multicenter trial in the United States. Mifepristone Clinical Trials Group." Arch Fam Med **7**(4): 360-6.
- Winikoff, B., I. Sivin, et al. (1997). "Safety, efficacy, and acceptability of medical abortion in China, Cuba, and India: a comparative trial of mifepristone-misoprostol versus surgical abortion." Am J Obstet Gynecol **176**(2): 431-7.
- Wong, K. S., C. S. Ngai, et al. (2000). "A comparison of two regimens of intravaginal misoprostol for termination of second trimester pregnancy: a randomized comparative trial." Hum Reprod **15**(3): 709-12.