MEDICAL ABORTION

BERNA DILBAZ
• 210 million women get pregnant annually
  – 15% miscarriages, stillbirths
  – 22% induced abortions
  – 63% live births
Abortion – a response to unwanted pregnancy

- 50 million abortions occur annually
- 20 million abortions are unsafe, usually illegal
- Every day more than 200 women die of unsafe abortion
Turkey

First Law on Population Planning

2nd Law on Population Planning
Legalizing abortion 10 weeks

1923
1965
1983
2011

First Law on Population Planning

Turkish Republic
### Distribution of Abortions

<table>
<thead>
<tr>
<th>Year</th>
<th>VTOP(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993 TDHS</td>
<td>18</td>
</tr>
<tr>
<td>1998 TDHS</td>
<td>14.5</td>
</tr>
<tr>
<td>2003 TDHS</td>
<td>11</td>
</tr>
<tr>
<td>2008 TDHS</td>
<td>10</td>
</tr>
</tbody>
</table>

**Spontaneous Abortion Rate:**

% 10.5
Abortions are decreasing in Turkey

![Graph showing the decrease in abortions in Turkey from 1983 to 2003. The graph indicates a decline in the number of abortions per 100 pregnancies, women, and live births over the years.](image)
The changes in total VTOP frequency per woman 1983-2008
Maternal Mortality between 1974-2005

Per 100,000 live births

1974: 208
1981: 132
1990: 100
1998: 49
2005: 28.5
2008: 19.5
2010: 16.4

12.1 in the west and 22.9 in the north-east in 2008

Distribution of maternal mortality according to gestational age

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>Last 2 yrs</th>
<th>2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;21 wks</td>
<td>3.9</td>
<td>2.6</td>
</tr>
<tr>
<td>22-31 wks</td>
<td>5.8</td>
<td>3</td>
</tr>
<tr>
<td>32-35 wks</td>
<td>1.1</td>
<td>1.5</td>
</tr>
<tr>
<td>36-37 wks</td>
<td>1.1</td>
<td>1.5</td>
</tr>
<tr>
<td>38+</td>
<td>5.2</td>
<td>62.8</td>
</tr>
</tbody>
</table>
Abortion rates in Eastern Europe
(abortions/1,000 women 15-44 yrs)

Abortion rates in Western Europe
(abortions/1,000 women 15-44 yrs)

Recommendations of the Council of Europe (2008)

The Assembly invites the member states of the Council of Europe to:

7.1. decriminalize abortion within reasonable gestational limits, if they have not already done so;

7.2. guarantee women’s effective exercise of their right of access to a safe and legal abortion;

7.3. allow women freedom of choice and offer the conditions for a free and enlightened choice without specifically promoting abortion;
What is medical abortion?

• A way of inducing termination of pregnancy with medicines (pills) without any surgical intervention
• A “no touch” procedure
• In history potions, teas, herbal remedies that women have sought for
• A new option and safe alternative to surgical abortion
Indications for abortion

• Legal induced abortion (in some countries)
• Fetal demise
• Fetal abnormality
• Exposure to teratogenic agents
• Mother’s medical status
Surgical Abortion

- Involves invasive procedure
- Usually requires one visit
- Complete in a predictable period of time
- Available during early pregnancy
- High success rate (99%)
- Does not require follow-up in all cases
- Patient participation in a single-step procedure
- Allows use of sedation if desired
Early Abortion with Vacuum Aspiration

• 17 of 1,132 women required re-aspiration
  – 1.5% of study population
  – 2.3% of follow-up population

• Of the 750 women who followed up, 13 experienced other complications:
  – 4 incomplete abortions
  – 2 unrecognized ectopic pregnancies
  – 1 hematometra
  – 4 pelvic infections
  – 3 re-aspirations for negative pathology

Paul et al. 2002
Features of Medical Abortion

- Usually avoids invasive procedure
- Requires two or more visits
- High success rate (95%)
- Requires follow-up to ensure completion of abortion
- Patient participation throughout a multiple-step process
- Usually avoids anesthesia
An overview of agents used for medical abortion

1) Prostaglandin analogues (Dinoprost, dinoprostone, carboprost, sulprostone, gemeprost, meteneprost & misoprostol)
2) Antiprogestogens (Mifepristone, Lilopristone & onapriston)
3) Epostane
4) Oxytocin
5) Methotraxate
6) Hypertonic Agents (Hypertonic saline and urea)
7) Etacridine lactate
   - Hydrophilic cervical dilatators (Laminaria, lamicel, dilapan)
   - Mechanical agents for cervical dilatation (foley catheter)
Currently available medical abortion regimens

- **Mifepristone** and a prostaglandin analogue (in the majority of the world, the analogue **misoprostol** is used)
- **Methotrexate** and **misoprostol**
- **Misoprostol** alone

\[
\begin{align*}
mifepristone & = \text{antiprogestin} \\
methotrexate & = \text{antimetabolite} \\
misoprostol & = \text{prostaglandin analogue}
\end{align*}
\]
History and Development of Medical Abortion

“RU 486 is the moral property of women”

- **1982-1988**: Sequential open-label trials in France to establish dose and safety of RU486.
- **1989**: Market Authorization granted
- **October 1989**: Roussel Uclaf/Hoechst decision to withdraw the product

Media campaign, advocacy asking Roussel Uclaf to reverse its decision

- French Health Minister Claude Evin forces company to retract its decision

  “RU 486 is the moral property of women”

April 1990: Mifépristone available on the market
Mifepristone Approval in Europe

1989 : France up to 7 weeks LMP
1991 : UK up to 9 weeks
1992 : Sweden up to 9 weeks
1997 : European registration up to 7 weeks
2007 : New European registration up to 9 weeks
2007 : Portugal (after the new law)
2009 : Italy (lot of restrictions)
Milestones in development

- Mifepristone discovered in 1980
- First clinical trial in 1982, Geneva
- Prostaglandins added, late 1980’s
- Some approvals
  - China: 1987
  - USA: 2000
  - South Africa, Taiwan, Tunisia: 2001
Where are we now in the world?

- Registrations in 35 countries
- Use by 2.5-3 million women outside of China
- Use by more than 22 million women in China
- High efficacy (92-97%)
- Excellent safety record
Global mifepristone approvals

Different colors represent the year when approved. Stripes indicate availability of combination pack products.

Not yet available in Turkey
<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Year</th>
<th>Country</th>
<th>Year</th>
<th>Country</th>
<th>Year</th>
<th>Country</th>
<th>Year</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td>China</td>
<td>1999</td>
<td>Austria</td>
<td>2000</td>
<td>Norway</td>
<td>2001</td>
<td>New Zealand</td>
<td></td>
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<tr>
<td></td>
<td>France</td>
<td></td>
<td>Belgium</td>
<td></td>
<td>Russia</td>
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<td>South Africa</td>
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<td></td>
<td>Denmark</td>
<td></td>
<td>Taiwan</td>
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<td>Uzbekistan</td>
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<tr>
<td>1991</td>
<td>UK</td>
<td></td>
<td>Finland</td>
<td>2001</td>
<td>India</td>
<td>2002</td>
<td>Azerbaijan</td>
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<td></td>
<td>Germany</td>
<td></td>
<td>Georgia</td>
<td></td>
<td>Belarus</td>
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<tr>
<td>1992</td>
<td>Sweden</td>
<td></td>
<td>Greece</td>
<td></td>
<td>US</td>
<td>2002</td>
<td>Moldova</td>
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<td></td>
<td></td>
<td></td>
<td>Israel</td>
<td></td>
<td>Latvia</td>
<td></td>
<td>Guyana</td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td>Luxembourg</td>
<td></td>
<td>Ukraine</td>
<td>2005</td>
<td>Albania</td>
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<td></td>
<td></td>
<td></td>
<td>Netherlands</td>
<td></td>
<td>Tunisia</td>
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<td>Hungary</td>
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</tbody>
</table>
Misoprostol Approved (2004)

approved

not approved

also approved for an ob/gyn indication

© 2005 Gynuity Health Projects
FDA approval provider qualifications in the U.S.

- Must be able to date the age of gestation
- Must be able to diagnose ectopic pregnancy
- Must be able to provide or arrange referral for surgical aspiration
- All capacities are self-certified
Usual way to use in the U. S.A

- Available in USA since 2000
- Registered for 600 mg mifepristone + 400 mcg oral misoprostol to 49 days LMP
- Most clinicians use 200 mg mifepristone + 800 mcg vaginal misoprostol to 63 days LMP
- Official label specifies 3 clinic/office visits but virtually all use is with misoprostol at home and only 2 visits (Schaff: 99% of over 4,000 patients)
Adverse events: regulatory

• Very low rate reported to FDA (0.17%)

• Most not serious (heavy bleeding; ongoing pregnancy)

• Infection 13/100,000 uses (Cl. Sordelli)
More than **1.3 Million** women used Mifeprex in the U.S. from September 2000 to May 2010.
Availability of mifepristone and abortion rate

Abortions per 1,000 women aged 15 to 45

Source: The Alan Guttmacher Institute New York
Provision of Medical Abortion in Europe

The provision of the method is shaped by the local policy, social and economic context as well as local health systems and medical practice

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>United Kingdom 2007</th>
<th>Netherlands 2006</th>
<th>Switzerland 2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>Sweden</td>
<td>35% England 61% Scotland</td>
<td>11,6 %</td>
<td>56%</td>
</tr>
<tr>
<td>2007</td>
<td>2007</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

49% 72%
Evolution of the percentage of MA since the commercialization in 1989 in France

In 2007, 49% of all abortion were medical abortion
Almost 90% of abortion less than 7 weeks LMP were medical abortion
Rationale to Moving Services away from Hospital Based

- MA is a simple procedure which can be easily and quickly learnt
- with high efficacy (92-97%) and excellent safety record (low risk of complication)
- No need to set up special facilities
What is mifepristone?

• Antiprogestin compound

• Licensed for pregnancy termination in 33 countries
Mifepristone

![Chemical structures of Mifepristone, Progesterone, and Norethindrone]
How does mifepristone work?

- Binds to progesterone receptor to block action of progesterone
- Increases endogenous prostaglandins
- Increases uterine contractility and sensitivity to prostaglandins
- Decidua and trophoblast separate
- Cervix softens and dilates, facilitating abortion
What is misoprostol?

• Prostaglandin E1 analogue
• Approved for prevention and treatment of gastric ulcers associated with the use of nonsteriodal anti-inflammatory drugs (NSAIDS)
• Causes contractions of smooth muscles of the uterus:
  – Reduces bleeding
  – Opens cervix
  – Empties uterus
Chemical Name: (±) methyl 11β, 16-dihydroxy-16-methyl-9-oxoprost-13E-en-1-oate
How does misoprostol work?

- Causes contractions of smooth muscles lining the uterus -> empties the uterus
- Softens the cervix -> increases dilation for intrauterine procedures, facilitates expulsions
## Misoprostol: routes of administration

<table>
<thead>
<tr>
<th>Route</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Rapid absorption (Peak 13-60 minutes)</td>
</tr>
<tr>
<td></td>
<td>Levels fall after 2 hours</td>
</tr>
<tr>
<td>Vaginal</td>
<td>Peak later, lower (80 minutes)</td>
</tr>
<tr>
<td></td>
<td>Detectable longer in plasma</td>
</tr>
<tr>
<td>Sublingual</td>
<td>Rapid absorption, high peak, sustained levels</td>
</tr>
<tr>
<td>Buccal</td>
<td>Later, lower peak, sustained levels, similar to vaginal</td>
</tr>
<tr>
<td>Rectal</td>
<td>Lower peak but higher levels longer than oral</td>
</tr>
</tbody>
</table>
Classic medical abortion regimen (French Regimen)

- Day 1: 600 mg mifepristone
- Day 3: 400 mcg oral misoprostol
- Day 15: follow up
Approved regimen and subsequent innovations

- Some innovations incorporated in current use
  - 600 → 200 mg mifepristone
  - Different routes of misoprostol administration: vaginal, buccal, sublingual
  - Use through 63 days’ gestation

\[
\begin{align*}
600 \text{ mg mifepristone} & \quad \text{Day 1} \\
400 \mu\text{g misoprostol p.o.} & \quad \text{Day 2} \\
\text{Follow-up visit} & \quad \text{Day 3} \\
\text{Additional follow up if necessary} & \quad \text{Day 15}
\end{align*}
\leq 49 \text{ days’ gestation}
\]
Regimen used in France

Official registered regimen is
D1 : 600mg mifpristone
D3 : 400µgmisoprostol oral in Practice

In Practice: 200mg mifepristone + 600 or 800 µg misoprostol sublingual or buccal
D15-21 : Follow up visit mainly with quantitative HCG level

Efficacy rate : 95-98%
Post-abortion uterus

Endometrial thickness of 15 mm or less is accepted as normal after abortion
• Misoprostol not registered for use in pregnant women but widely used off-label with mifepristone for medical abortion in most countries.
• Mifepristone has limited availability
• Mifepristone is the most expensive of these drugs because of relatively complex synthesis – small-scale and low yield; and small sales volumes.
An affordable product of assured quality

**Combipack of Mifepristone Tablets and Misoprostol Tablets**

**MEDABON**

Each blister pack contains:
(A) Yellow uncoated tablet containing
Mifepristone 200 mg
(B) White uncoated tablet containing
Misoprostol 200 mcg

Dosage and Administration:
200 mg of Mifepristone (1x200mg Tablet) in a single oral dose, followed 36 - 48 hours later by 800mcg of misoprostol (4x200 mcg Tablets) in a single dose given vaginally. The dosage is independent of body weight. If the patient vomits shortly after administration of the mifepristone, she should inform the doctor.

Warning: Keep out of reach of children.

FOR CLINICAL TRIAL USE ONLY

Storage: Store at or below 25°C (77°F), in a dry area.

GUJ/DRUGS/25/789

Return empty packaging and unused products

* Trade Mark

Manufactured by:
Sun Pharmaceutical Industries Limited,
Halol-Baroda Highway,
Halol : 389 350, Gujarat, INDIA,

DAY 1
FIRST DOSE ORALLY

36-48-HOURS AFTER FIRST DOSE-VAGINALLY
• Price – Co-packaged product <US$3.75 fob Mumbai to public sector, making it affordable to many more women.
• Quality - Manufactured in USFDA/EMEA compliant facility, meeting international current Good Manufacturing Practice (cGMP).
• Regulatory issues – Misoprostol used “off-label”, regulatory agencies welcome formal registration of misoprostol for use in medical abortion; – clinical part of registration dossier based on WHO clinical trials.
• Ease of use – co-packaged product easier for both provider and woman.
Mifepristone + Misoprostol protocols used for medical abortion

- Misoprostol is given 48 hrs after Mifepristone administration.
- Abortion is completed in 90% of the patients 4-6 hours after Misoprostol administration.
- Sublingual use of Misoprostol is related more with gastrointestinal side-effects while diarrhea can be observed in buccal use.
Mifepristone + Misoprostol protocols used for medical abortion

- Sublingual use of Misoprostol is related more with gastrointestinal side-effects while diarrhea can be observed in buccal use.
- The success of the procedure is 95-98% in pregnancies up to 9 weeks.
- In 2-5% of the women surgical intervention is required due to ongoing pregnancy, incomplete abortion or bleeding.
<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Mifepristone (Mife) dosage</th>
<th>Misoprostol (Miso) dosage, route and timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 9 weeks</td>
<td>200 mg oral (400-600 mg)</td>
<td>Single dose buccal or sublingual or vaginal 800 µg 48 hours after Mife. (Oral route 400 µg can be used up to 7 weeks of gestation)</td>
</tr>
<tr>
<td>9-12 weeks (Terminations for medical reasons, missed abortion)</td>
<td>200 mg oral (400-600 mg)</td>
<td>800 µg vaginal 48 hrs after Mife, followed by 400 µg vaginal or sublingual Miso every 3 hours up to 4 doses</td>
</tr>
<tr>
<td>&gt;12 weeks (Terminations for medical reasons, missed abortion)</td>
<td>200 mg oral (400-600 mg)</td>
<td>400 µg oral or 800 µg vaginal, 48 hrs after Mife followed by 400 µg vaginal or sublingual Misoprostol every 3 hours up to 5 doses</td>
</tr>
</tbody>
</table>
## Contraindications for Mifepristone + Misoprostol regimens:

<table>
<thead>
<tr>
<th>Contraindication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy to Mife or Miso or other prostaglandins</td>
</tr>
<tr>
<td>Diagnosed or query of ectopic pregnancy</td>
</tr>
<tr>
<td>Porphiria</td>
</tr>
<tr>
<td>Bleeding disorders or anticoagulant use</td>
</tr>
<tr>
<td>Asthma with systemic corticosteriod use (Mife blocks the effect of steroids)</td>
</tr>
<tr>
<td>In case of in-utero IUD presence IUD should be removed prior to medication. Caution must be taken in women with sever anemia, serious medical disorder or women on longterm steroid use</td>
</tr>
</tbody>
</table>
Mife + Miso regimens: Route of Misoprostol

- Vaginal administration was the original route used in the evidence-based regimen
- Women prefer oral to vaginal route + vaginal route related with Clostridium Sordelli infections
- Oral an buccal routes are acceptable for women
- Sublingual route can be used
Misoprostol-only regimens

• Single use of Misoprostol is not as successful as the Mife + Miso regimens. Misoprostol dosage must be reduced in advanced pregnancies.

• In cases of incomplete abortion (<13 gestational week) single dose 600 µg oral or 400 µg sublingual Misoprostol can be used.
<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Misoprostol dosage and route</th>
<th>Timing of repeated dosages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 12 weeks (induced abortion up to 10 weeks, induced abortions for medical indications, missed abortion)</td>
<td>800 µg sublingual or vaginal</td>
<td>If abortion is not completed after the initial dose 800 µg sublingual or vaginal misoprostol every 3 hours up to 3 repeated dosages and overall 12 hours.</td>
</tr>
<tr>
<td>&gt;12 weeks (Induced abortions for medical indications Missed abortion)</td>
<td>400 µg sublingual or vaginal</td>
<td>Sublingual or vaginal 400 µg Misoprostol every 3 hours maximum 5 dosages until abortion is completed.</td>
</tr>
</tbody>
</table>
**Contrendications for Misoprostol use:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy to Miso or other prostaglandins</td>
<td></td>
</tr>
<tr>
<td>Diagnosed or query of ectopic pregnancy</td>
<td></td>
</tr>
<tr>
<td>Bleeding disorders or anticoagulant use</td>
<td></td>
</tr>
<tr>
<td>In case of in-utero IUD presence</td>
<td>IUD should be removed prior to medication. Caution must be taken in women with severe anemia, serious medical disorder or women on longterm steroid use</td>
</tr>
</tbody>
</table>
Counselling for medical abortion:

- Medical abortion simulates spontaneous abortion, it is like menstruation when used in early pregnancies.
- Bleeding, pain and other side-effects should be explained to the women.
- Bleeding begins 1-3 hours after Miso and could continue up to 4 hours after the medication.
Counselling for medical abortion:

- Cramping pain begins 30 minutes after Miso, the intensity of pain varies
- Painkillers should be given before the cramps begin
- Ibubrufen or paracetamol (maximum 4 grams/24 hours)
- Hot towel or hot water application
- Antibiotic prophylaxis should be given to women with a risk of infection
DANGER SİGNİS:

• Excessive bleeding (more than 2 pads per hour) accompanied by diziness, fatigue
• Temperature >38ºC especially if it occurs 24 hours after Misoprostol Foul smelling discharge
• Excessive cramping and abdominal pain
200 vs. 600 mg of Mifepristone

• Drug provided as 200 mg tablets
• WHO study shows two doses similar:
  88.1% (600 mg) vs. 89.3% (200 mg)
• Extra tablets not necessary
  - Mifepristone is expensive; using less would reduce cost a lot
  - Clinical studies and use clearly show higher dose is not needed.
Failure Rates by Gestational Age
Regimens of Mifepristone-Misoprostol

49 days ≤ 50-56 days 57-63 days

- Schaff 200mg mife/800mcg miso P.V.
- Ashok 200mg mife/800mcg miso P.V.
- Spitz 600mg mife/400mcg miso P.O.
- Aubeny 600mg mife/400mcg miso P.O.
- WHO 600/200mg mife/400mcg miso P.O.
Many regimens work well

<table>
<thead>
<tr>
<th>Dose mifepristone</th>
<th>Dose misoprostol</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>600 mg</td>
<td>400 mcg oral misoprostol</td>
<td>Labeled in India, the U.S., South Africa, France and most other European countries</td>
</tr>
<tr>
<td>200 mg</td>
<td>400 mcg oral misoprostol</td>
<td>Used in Tunisia, Vietnam, some in the U.S. and increasingly in France</td>
</tr>
<tr>
<td>200 mg</td>
<td>800 mcg vaginal misoprostol</td>
<td>Most used regimen in the U.K., Sweden, and the U.S.</td>
</tr>
<tr>
<td>150 mg (in divided doses)</td>
<td>600 mcg oral misoprostol</td>
<td>Most commonly used regimen in China</td>
</tr>
</tbody>
</table>
Maedical Abortion Regimens in USA

• FDA approved/manufacturer-recommended regimen – **Mifepristone** (600 mg orally), followed 48 hours later by **misoprostol** (400 mcg orally (clinician))

• Evidence-based regimen – **Mifepristone** (200 mg orally) administered by a clinician, followed 24 to 72 hours later by **misoprostol** (800 mcg buccally) administered either by a healthcare provider or self-administered in a nonclinical setting, typically the patient’s home.
SPECIAL COMMUNICATION

A consensus regimen for early abortion with misoprostol

N.M. Philip\textsuperscript{a}, B. Winikoff\textsuperscript{a,\ast}, K. Moore\textsuperscript{b}, P. Blumenthal\textsuperscript{c}

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\textsuperscript{b}Reproductive Health Technologies Project, Washington, DC, USA
\textsuperscript{c}Johns Hopkins Bayview Medical Center, Baltimore, MD, USA

Received 7 April 2004; received in revised form 25 August 2004; accepted 25 August 2004

KEYWORDS
Misoprostol; Abortion; Medical abortion; Pregnancy termination

Misoprostol, a widely available, inexpensive prostaglandin E\textsubscript{1} analog, is marketed (commonly as Cytotec\textsuperscript{\textregistered}, Pfizer but also other brands) for prevention and treatment of gastric ulcers. The scientific literature supports use of misoprostol as a treatment for many women’s reproductive health indications. Perhaps most notably, the drug has been useful for pregnancy termination because of its uterotonic properties. The pharmaceutical entity holding the original misoprostol patent (Searle) declined to develop misoprostol for women’s health, including for termination of pregnancy. Instead, efforts were undertaken by individual researchers acting alone, so that there is no consensus on recommended regimens for abortion and a lot of ad hoc use [1,2]. Mifepristone-misoprostol regimens have clear advantages over misoprostol alone for early abortion in efficacy and side-effects [3,4], but where mifepristone is not available, lack of consensus on use of misoprostol alone may prevent access to an alternate abortion method and, sometimes, to an opportunity to avoid unsafe abortion [5].

An expert meeting was convened to determine whether a safe, effective misoprostol alone regimen can be recommended for pregnancy termination in early gestation. The gathering assembled experts on use of misoprostol for early abortion, representatives of training and advocacy organizations, and leading obstetrician–gynecologists. The task of the group was to establish clinical guidelines for early abortion with misoprostol alone.

After careful review of the literature and discussion of the clinical aspects of varied regimens, participants developed a consensus statement, entitled Instructions for Use—Abortion Induction with Misoprostol in Pregnanacies through 9 Weeks LMP [6] (See Appendix A), to be used as the basis for training and for information materials for providers and advocates. Copies of this consensus...
Four cases of death was reported from USA in women who used Mifeprex (mifepristone) and vaginal misoprostol (2 cases in 2003, 2004, 2005).

Toxic shock and endometrial infection with isolation of Clostridium sordelli in 2 cases.

A similar case reported from Canada in 2001.

C. sordelli infection is rare, features are: toxic shock, hypotension, effusion, hemoconcentration and leucocytosis.
Mifepristone – infection?

• Mifepristone blocks progesterone & glucocorticoid receptors
• Effects cortisol ve cytokin secretion
• Immune system is effected and this enables endometrial invasion of C.sordelli
• Endo and exotoxin excretion caused by C.sordelli lead to fatal septic shock
• No. Of cases restricted so etiology ?

Meich RP, Ann Pharmacother. 2005
Medical abortion and week of pregnancy

Up to 9 weeks:
• Mifepristone + misoprostol
• MTX +/- Miso
• MTX better than Miso (Aldrich&Winikoff,2007)
• MTX is effective but not recommended by WHO due to its teratogenic effects

9-12 weeks:
• Mifepristone + misoprostol
• Misoprostol alone
• Gemeprost alone

After 12 weeks:
• Misoprostol or Gemeprost alone
Frequent low dose (100 µg-miso/2 hrs) – a pharmacokinetic based use in 13-20 weeks

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction to expulsion (hrs)</td>
<td>12.5 ± 5.9 (2-42)</td>
</tr>
<tr>
<td>Total misoprostol dose (µg)</td>
<td>728 ± 297 (200-2100)</td>
</tr>
<tr>
<td>Augmentetion with oxytocin (%)</td>
<td>5 (2.8 %)</td>
</tr>
<tr>
<td>Abortion &lt; 24 hrs (%)</td>
<td>245 ( 98 %)</td>
</tr>
<tr>
<td>Foley catheter (%)</td>
<td>5 (2 %)</td>
</tr>
<tr>
<td>Placental retansion (%)</td>
<td>7 ( 2.8 %)</td>
</tr>
<tr>
<td>Pain management (%)</td>
<td>41 ( 16.4 %)</td>
</tr>
</tbody>
</table>

_Dilbaz et al, Eur J Contracept Rep Health Care, 2004_
Increasing women's choices in medical abortion: a study of misoprostol 400 microg swallowed immediately or held sublingually following 200 mg mifepristone.

Ayse Akin¹, Rasha Dabash², Berna Dilbaz³, Hale Aktun⁴, Polat Dursun¹, Sibel Gokkurt¹, Bahar Dogan¹, Beverly Winikoff²

1. Hacettepe University School of Medicine, Ankara, Turkey
2. Gynuity Health Projects, New York, USA
3. MOH Etlik Hospital, Ankara, Turkey
4. ZTB Maternity Hospital, Ankara, Turkey
Success rate with 200 mg mifepristone + 400 µg misoprostol (48 hrs) (N=207)

<table>
<thead>
<tr>
<th>Overall success (%)</th>
<th>95.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete abortion/unnecessary intervention</td>
<td>2.9</td>
</tr>
<tr>
<td>Ongoing pregnancy</td>
<td>1.9</td>
</tr>
</tbody>
</table>

**Success- route of Miso (%)**

<table>
<thead>
<tr>
<th>Sublingual (n=46)</th>
<th>90.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral (n=161)</td>
<td>98.1</td>
</tr>
</tbody>
</table>
Medical abortion, is an option for women who wish to terminate a first-trimester pregnancy. It is most commonly used up to 63 days of gestation (LMP), the treatment also is effective after 63 days of gestation. CDC estimates that 64% of abortions are performed before 63 days of gestation. 6.5% of all abortions in USA are medical abortions, (25.2% of all abortions at or before 9 weeks of gestation ) Mifepristone, combined with misoprostol, is the most commonly used medical abortion regimen in the United States and Western Europe.
Mife + other prostoglandins:

- Other prostaglandins are inferior to misoprostol.
- Gemeprost vaginal pessary is expensive, needs to be refrigerated, and is not registered for use in USA, associated with more treatment failures than misoprostol.
- Sulprostone, is associated with cardiovascular adverse effects.
Medical Abortion and patient satisfaction:

• Medical Abortion 82% vs Surgical abortion under general anaesthesia 92% (side-effects effected patient satisfaction) (Rebrye et al Hum Reprod 2005)

• Higher proportion of women who underwent MA would choose the same method if a future abortion was required (81 versus 58 percent in the surgical abortion group (Jensen et al Am J Obstet Gynecol. 2000))
Side-effects of Mife + Miso Regimens:

- Gastrointestinal discomfort (nausea 34-72%, vomiting 12-41%, diarrhea 3-22%) only 20% of these symptoms are severe. GI symptoms oral, > gestational age
- Pain
- Excessive vaginal bleeding.
- Some women experience headache, dizziness, or fatigue.
- Rarely surgical intervention may be required to terminate the pregnancy if side effects are poorly tolerated
Significant adverse events and outcomes after medical abortion. Obstet Gynecol. 2013

- Planned Parenthood affiliates data (2009-2010), out of 233,805 medication abortions:
  - Significant adverse events or outcomes 0.65%.
- The complication rate for medication abortion is similar to surgical abortion, but the types and etiologies of the complications are different.
- Endometritis has a similar incidence as in surgical abortion; overall infection rate is low (0.016%); life-threatening infections are rare, but have occurred more often than with surgical abortion.
- Hemorrhage occurs at similar rates, but the cause is typically uterine atony or retained products of conception rather than the causes in surgical abortion, which are usually cervical laceration or uterine injury due to instrumentation.
• Case fatality rate $0.6/100,000$ legal induced abortions) and is much lower than that of pregnancy ($12$ maternal deaths/$100,000$ live births)

*Stubblefield PG et al 2004, Elam-Evans LD et al 2003*
MA and Teratogenicity

Surgical abortion should be performed in case of failure with MA due to teratogenicity related to Misoprostol, medical supervision is required:

- Cranial nerve defects (especially pairs 6 and 7, characteristic of the Möbius syndrome)
- Limb abnormalities
- Möbius syndrome
The efficacy varies with several factors:

- Gestational age
- Route and dose of misoprostol administration
- Parity – The rate of successful abortion is lower with increasing parity and in women who have had a previous abortion (Spitz N Eng J Med 1998)
Key service delivery issues in medical abortion

- Type of provider
- Level within health care system
- Use of ultrasound
- Pain management
- Information/counseling
- Clinic environment
- Almost all regimen choices


Websites:
• Gynuity Health Projects
• International Consortium on Medical Abortion
• medicationabortion.org maintained by Ibis Reproductive Health
• The National Abortion Federation
• International Planned Parenthood Federation
• womenonweb