CONTRACEPTION: NEW OPTIONS AND DELIVERY SYSTEMS

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## DISCLOSURES: Paula J. Adams Hillard, M.D.

<table>
<thead>
<tr>
<th>Type of Affiliation/ Financial Relationship</th>
<th>Name of Corporate Organization</th>
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<tr>
<td>Consultant or Scientific Advisory Board</td>
<td>Procter &amp; Gamble, Wyeth-Ayerst, Merck, Glaxo</td>
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<td>Grant/Research Support</td>
<td>Berlex, Wyeth-Ayerst, Duramed</td>
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<td>Speaker’s Bureau</td>
<td>Wyeth-Ayerst, Berlex, Merck, ARHP, Pharmacia-Upjohn, 3-M Pharmaceuticals, Pfizer, Organon, Ortho-McNeill, Barr Labs, Tap Pharmaceuticals</td>
</tr>
</tbody>
</table>
A Different Perspective On The Challenges Of Contraception And Compliance

Women of reproductive age: 600 million
Number of acts of intercourse: 39 trillion
Ejaculations per second: 12,000
Sperm per ejaculate: 60 million

Total worldwide sperm release = 720 trillion sperm per second
THE FUTURE IS NOW....

New Options in Contraception

FINALLY

Why do we need new options in contraception?
Average Reproductive Time Line

- Menarche: 10 years
- First Intercourse: 12.8 years (12.2 AA)
- First Marriage: 17.7 years
- First Birth: 22.6 years
- Desired Family Size: 24.3 years
- Menopause: 28.3 years

Reproductive Concerns:
- Postponing
- Spacing
- Completed Family
AVERAGE REPRODUCTIVE TIME LINE

The typical woman spends five years pregnant, postpartum or trying to get pregnant and 30 years avoiding pregnancy.

Guttmacher Institute. 2006. Abortion in Women’s Lives
Intended vs. Unintended Pregnancy in U.S.

Henshaw SK, *Family Planning Perspectives*, 1998
U.S. Pregnancies: Unintended vs. Intended (Women of all Ages)

Intended 51%

Unintended 49%:
- Unintended births 22.5%
- Elective Abortions 26.5%

UNINTENDED PREGNANCIES (%) BY AGE

Direct medical costs of unintended pregnancy

$5.0 Billion in 2002

<table>
<thead>
<tr>
<th>Age</th>
<th>%</th>
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<tbody>
<tr>
<td>15-19</td>
<td>78</td>
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<tr>
<td>20-24</td>
<td>58.5</td>
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<tr>
<td>25-29</td>
<td>38.7</td>
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<td>30-34</td>
<td>33.1</td>
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<tr>
<td>35-39</td>
<td>40.8</td>
</tr>
<tr>
<td>40+</td>
<td>50.7</td>
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</table>

The Cost of Unintended Pregnancy in the United States

- Direct medical costs of unintended pregnancy
  - $5.0 Billion in 2002
- Direct medical cost savings due to contraceptive use $19.3 Billion

Trussell, J. Contraception 2006. 75 (3):168-70
Age at Time of Unintended Pregnancy

Alan Guttmacher Institute; Sex and America’s Teenagers 1994
ADOLESCENT PREGNANCY, BIRTH, AND ABORTION RATES


* Pregnancy and abortion data available only through 1997.

DECLINING ADOLESCENT PREGNANCY RATES....WHY?

- Estimates that increase in Abstinence accounted for 25%
- 75% of decline due to increased Use of contraceptives
  - Slight increased use of condoms
  - Significantly decreased use of OCs
  - Increased use of long-acting agents
  - From 0-13% resulting in 9% decrease in contraceptive failures

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U.S. ADOLESCENT PREGNANCY RATES

• Pregnancy rates 2-3x higher than in Canada and Europe
• Similar rates of sexual activity
• Lower rates likely due to:
  • Better education
  • Better reproductive health services
  • Better use of birth control,
    In particular, OCs


The Need for Contraception

Pregnancies Ending in Abortion by Age

On the basis of current abortion rates, one in three American women will have had an abortion by age 45.

Percent

0 10 20 30 40 50

15-19 20-24 25-29 30-34 35-39 40+

Age (y)

*Does not include miscarriages.

www.contraceptiononline.org
http://www.guttmacher.org/in-the-know/incidence.html
Trends in overall contraceptive use

Contraceptive prevalence rates

(Source: UN Population Division, 1991, 1999 and 2001)
Estimates of annual incidence of unsafe abortion, around the year 2000

Total number= 19 million

- Africa: 4.2 million
- Latin America and Caribbean: 3.7 million
- Europe: 0.5 million
- Asia: 10.5 million

(Source: WHO, 2002)
CONTRACEPTION

Prevents Unintended Pregnancies AND Abortions
"We discover more and more each day that protests and pickets don't stop abortion; birth control and responsible sex educators do."

—

"I do not pretend that birth control is the only way in which population can be kept from increasing. There are others, which, one must suppose, opponents of birth control would prefer."

"Those who in principle oppose birth control are either incapable of arithmetic or else in favor of war, pestilence and famine as permanent features of human life"

Bertrand Russell
REALITY:
No contraceptive method is perfect, even when used consistently and correctly

Direct medical cost savings due to contraceptive use: $19.3 Billion
CONTRACEPTIVE EFFICACY:
How Well Will it Work?
Everything you Always Wanted to Know about Contraception….But were Afraid to Ask
<table>
<thead>
<tr>
<th>METHOD</th>
<th>% unintended preg/1st yr</th>
<th>Trussell 2004</th>
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<tbody>
<tr>
<td></td>
<td>Typical Use</td>
<td>Perfect Use</td>
</tr>
<tr>
<td>COC and POP</td>
<td>8</td>
<td>0.3</td>
</tr>
<tr>
<td>Patch</td>
<td>8*</td>
<td>0.3*</td>
</tr>
<tr>
<td>Vaginal Ring</td>
<td>8*</td>
<td>0.3*</td>
</tr>
<tr>
<td>Condom Male</td>
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<td>2</td>
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<tr>
<td><strong>No Method</strong></td>
<td><strong>85</strong></td>
<td><strong>85</strong></td>
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<tr>
<td>DMPA</td>
<td>3</td>
<td>0.3</td>
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<tr>
<td>Withdrawal</td>
<td>27</td>
<td>4</td>
</tr>
<tr>
<td>Implant</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>Periodic abstinence</td>
<td>25</td>
<td>1-9</td>
</tr>
<tr>
<td>Spermicides</td>
<td>29</td>
<td>18</td>
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</table>
Comparing effectiveness of methods

More effective
Less than 1 pregnancy per 100 women in one year

- Implants
- Vasectomy
- Female Sterilization
- IUD

How to make your method most effective

After procedure, little or nothing to do or remember
- Vasectomy: Use another method for first 3 months
- Injections: Get repeat injections on time
- LAM (for 6 months): Breastfeed often, day and night
- Pills: Take a pill each day
- Patch, ring: Keep in place, change on time

Less effective
About 30 pregnancies per 100 women in one year

- Male Condoms
- Female Condoms
- Diaphragm
- Fertility-Awareness Based Methods
- Withdrawal
- Spermicide

Condoms, diaphragm: Use correctly every time you have sex
Fertility-awareness based methods: Abstain or use condoms on fertile days. Newest methods (Standard Days Method and Two Day Method) may be easier to use.
Withdrawal, spermicide: Use correctly every time you have sex

TRENDS IN CONTRACEPTIVE USE NSFG

Ever-Use, All Ages

CONTRACEPTIVE CONSIDERATIONS

- Efficacy/Reliability
- Convenience
- Reversibility
- Prevention of STDs
- Cost
- Safety/Perceived Safety
- Partner preference/Cooperation
- Side effects—Real and feared
- Effects on menstrual cycle
Cost Estimates of Contraception & Pregnancy over 5 Years

Cost vs Effectiveness at 5 years

HORMONAL METHODS OF CONTRACEPTION

- Oral Contraceptives
  - Low Dose
  - Generics
  - Continuous/Extended Cycle
- DMPA
- (Injectable Combination)
- Implant
- Vaginal Ring
- Transdermal patch
- Emergency Contraception
- IUS
Oral Contraceptives

- Lower dose combinations
- 20, 15, 10 ug Ethinyl Estradiol
ORAL CONTRACEPTIVE REGIMEN

- Traditionally 21/7 hormonally active/placebo
  - Arbitrary
  - Not a real “menstrual period”, but “withdrawal bleed”

- Extended cycle has been used for many years:
  - Honeymoon/vacation/athletic events
  - By female physicians
ORAL CONTRACEPTIVE REGIMENS

• Newer regimens
  • 24/4
  • 84/7 or 84/7*
  • 365

• Scheduled vs Unscheduled bleeding
  • Patient preference for bleeding
  • Bleeding vs spotting

• Monthly bleeding = “Monthly pregnancy test”
NEW PILL REGIMENS
24/4
Shorter Pill-free Interval Can Decrease Follicular Development

Percentage of Women with Follicular Development (↑ Follicle Size, ↑ E2, → or ↑ P) using 21- or 24-day Regimens

<table>
<thead>
<tr>
<th></th>
<th>1st Cycle</th>
<th>2nd Cycle</th>
<th>3rd Cycle</th>
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<tr>
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<td><img src="image2" alt="Bar" /></td>
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<tr>
<td>24-day regimen</td>
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Seasonique Bleeding Profile

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<tr>
<th>Cycle</th>
<th>&gt;= 7 days</th>
<th>&gt;= 20 days</th>
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<tr>
<td>1st</td>
<td>60</td>
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<td>2nd</td>
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<td>20</td>
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<td>3rd</td>
<td>30</td>
<td>10</td>
</tr>
<tr>
<td>4th</td>
<td>40</td>
<td>10</td>
</tr>
</tbody>
</table>
LYBREL Bleeding Profile

Women* with cumulative amenorrhea, bleeding, or spotting

- **Amenorrhea**
- **Spotting not requiring sanitary protection** (as determined by study subjects)
- **Bleeding requiring sanitary protection**

*779 subjects with complete data on bleeding experience for all 13 pill packs were used in the cumulative analysis.
Oral Contraceptives

- Bi-, Tri-cycling, Quadra-cycling
  - Endometriosis, anemia, fibroids, DUB, PMS, headaches, dysmenorrhea
- Barr Laboratories—Seasonale, Seasonique
  - 84/7-day cycles
  - Available since 2003
  - Seasonique—estrogen replaces placebos
“It’s Just for Quality of Life……..”
CANDIDATES FOR EXTENDED CYCLING

- Menstrual molimina
- Menstrual exacerbation of underlying disease
  - Seizure disorders
  - Hematologic diseases
- Endometriosis
- Athletes
- Mentally and physically challenged
- Hormone therapy (POF)
- Patient Choice

http://www.contemporaryobgyn.net
OCs and The Real World
FDA Panel January 2007

- Design of clinical trials
- Clinical trials should reflect the Real World of OC users
  - US women
  - Heavy women
  - Smokers
  - Adolescents
- Efficacy/Effectiveness: Pearl Index = # Pregnancies/100 women-years should be replaced by life-table analyses
  - Lower dose OCs
  - Overweight/Obese women
- Encouragement to use Electronic rather than paper Diaries
- Definitions of Bleeding/Spotting
  - Extended cycles
MEDICAL CONDITIONS IN WHICH THERAPEUTIC AMENORRHEA MAY BE DESIRABLE

• Hematologic Disease
  • Inherited Anemias (SS, Thalassemia, Fanconi’s)
  • Inherited Bleeding Disorders (VW dis, hemophiliases)
  • Anticoagulation
  • Malignancy requiring Chemo, BMT
  • Other—ITP, mobilized military personnel, cycle-exacerbated diseases. etc
MEDICAL CONDITIONS IN WHICH THERAPEUTIC AMENorrhea MAY BE DESIRABLE

• Other
  • Mobilized military personnel
  • Treatment of any severe, recurrent menstrual cycle-related disease exacerbation
PUBLIC AWARENESS

IS MENSTRUATION OBSOLETE?

How suppressing menstruation can help women who suffer from endometriosis, fibroids, PMS.

ELSIMAR M. COUTINHO

1999
WHAT DO WOMEN REALLY WANT?
“If you could choose the number of times you have your period each year while remaining healthy, what would be your preference?”

July-August 2002 ARHP Harris Poll

Results: http://www.arhp.org/healthcareproviders/visitingfacultyprograms/extended/nationalsurvey.cfm
Preferred Menstrual Frequency
2002 Harris Poll: ARHP

- 18-24 years (n=101)
- 25-29 years (n=45)
- 30-39 years (n=150)
- 40-49 years (n=195)

- Frequency categories: q mo, q 0 mo, q 3 mo, q 6 mo, q yr, never
Preferred Frequency of Menstruation

- **Ages 15-19 (n=321)**
- **Ages 25-34 (n=324)**
- **Ages 45-49 (n=319)**

**% of Respondents**

- Once per month
- Once every 3 months
- Once every 6 months
- Once a year
- Never

Den Tonkelaar I, Oddens BJ. Contraception. 1999;59:357-62
INTERNATIONAL PERSPECTIVE
Women’s Attitudes

Glasier AF et al. Contraception 67 (2003) 1-8
EXTENDED CYCLING
Why would women choose less frequent Periods?

- Menstrual Symptoms (Molimina)¹
  - Dysmenorrhea
  - Menstrual Headaches
  - Menorrhagia
  - PMS

- Ovulatory Cycles

¹Molimina: the periodic conscious manifestations (as tension or discomfort) associated with the physiological stress or effort involved in menstruation
Negatives of Menstruation

- Physical pain: back pain, abdominal and pelvic pain, bloating, headache, mastalgia, pain in limbs, irritability, lethargy, and depression
- Hygiene challenges—”on the rag”
- Women unclean—excluded from household, religious or community functions
- Limitation in achievements or opportunities
  - Dysmenorrhea is the single greatest cause of lost days of work and school in women < 25 yo
Terms/Slang for Menses

- “A visit from Aunt Flo”
- “That time of the month” / “Monthlies”
- “Falling off the roof”
- “The Curse”
- “Floodgates open up”
- “Leaky Faucet”
- “My sick time”
- “Falling to the Communists”

Museum of Menstruation and Women’s Health
http://www.mum.org/
WORK LOSS

• National Health Interview Survey 1999

• 2805 women—18-64 years old
  • 373 self-described heavy flow
  • 2432 self-described normal flow

• Women with heavier flow are 72% as likely to be working

• CONCLUSION: Menstrual bleeding has significant economic implications for women in the workplace:
  • Work loss from heavy flow estimated at $1692 annually per woman.

Cote I et al. Work loss associated with increased menstrual loss in the US. Obstet Gynecol 2002;100:683-7
Despite all the Pain and Suffering, Many women and Men Believe…

- Menstruation is natural
- Menstruation is necessary to cleanse "purge" the body
- Menstruation is healthy
- Menstruation endows women with mystical power
AMENORRHEA

- While taking HORMONAL THERAPY
- WITHOUT hormonal therapy
HEALTH RISKS OF EXTENDED CYCLE COCs ??

Cumulative Yearly Doses of LNG/EE Contained in Some OCs

- Cumulative EE and LNG doses were calculated by multiplying the number of active pills in 1 calendar year by the daily dose of active pills
- LYBREL provides women with more hormonal exposure on a yearly basis (13 additional weeks of hormone intake per year) than conventional cyclic oral contraceptives containing the same strength of synthetic estrogens and similar strength of progestins

HEALTH RISKS OF EXTENDED CYCLE COCs ??

• FDA approval
• No evidence of endometrial hyperplasia
• Long term effects not yet documented
QUESTIONS WOMEN ASK

- DOES IT WORK?
- IS IT SAFE?
- IS IT A GUARANTEE?
Extended-Cycle OC Trial:
Scheduled Withdrawal Bleeding/Spotting

Median number of scheduled withdrawal bleeding days per year

No “Pay back” or “Periods from Hell”

<table>
<thead>
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<th>Regimen</th>
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<tr>
<td>91-day regimen</td>
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<tr>
<td>28-day regimen</td>
<td>36</td>
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Extended-Cycle OC Trial: Unscheduled Bleeding/Spotting Days

Median number of unscheduled bleeding/spotting days per year

Extended-Cycle OC Trial: Unscheduled and Scheduled Bleeding/Spotting Days

Median number of unscheduled plus scheduled bleeding/spotting days per year

Extended-Cycle OC Trial: Median Days of BTB/Spotting

<table>
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<th>Cycle</th>
<th>(Days)</th>
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<th>4</th>
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<tr>
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<td>(1-84)</td>
<td>12</td>
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<td>6</td>
<td>4</td>
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<tr>
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<td>(92-175)</td>
<td>6</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(183-266)</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(274-357)</td>
<td>4</td>
<td></td>
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</tbody>
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FAILURE RATE OCs--FIRST YEAR
By Age and Income

AGE

<=19  20-24  25-29  >=30

% Pregnant

<=19  13  15  13  10
20-24  6  7  6  10
25-29  5  4
>=30

<=19  20-24  25-29  >=30

AGI, Sex and America’s Teenagers, 1994
THE MOST DIFFICULT ASPECT OF TAKING ORAL CONTRACEPTIVES...
ORAL CONTRACEPTIVE COMPLIANCE

• Incorrect Use
  • Missed pills
  • Runs out/ restarts late
  • Errors in use
    • Backwards
    • 21 days continuously
    • Placebo pills first
    • Problems with correct start
    • Transition errors from one pack to the next

• Discontinuation
  • On-again/ Off-again use
OC MICROBEHAVIORS

Takes a pill q d  Takes pill same time q d  Takes pills in same order  Takes all pills  Uses backup if forgets  Takes only own pills  Perfect Use

Oakley, Fam Plann Persp, 1991
COMPLIANCE AMONG OC USERS

Oral Contraceptives for Non-Contraceptive Indications

- “On-label”
- Acne indication
  - Estrostep
  - Ortho Tri-Cyclen
- Alesse
- Yaz

"If you decide to take the Pill, why not take the only one that's clinically proven to help your skin look better too?"
Noncontraceptive Benefits of OCs

- **Cycle-related:**
  - Irregular cycles
  - Dysmenorrhea
  - Menorrhagia
  - Anemia
  - Functional ovarian cysts

- **Cancer reduction:**
  - Ovarian
  - Endometrial
  - Colorectal?

Adapted from Grimes DA et al, eds. *Modern Contraception: Updates from The Contraception Report*. Emron;1997:1-100
Noncontraceptive Benefits of OCs

- **Prevention of:**
  - Bone loss
  - Fibrocystic/benign breast disease
  - Pelvic inflammatory disease (PID)
  - Ectopic pregnancy
  - Infertility

- **Treatment of:**
  - Acne
  - Hirsutism
  - Perimenopausal symptoms

Newer Progestin and New Indications

- 20 ug EE and 3 mg Drospirenone
- “Three indications”
  - Contraception
  - Acne
  - PMDD
- Mild antimineralocorticoid activity:
  - Reduced fluid retention?
  - Weight neutral
  - Androgen excess disorders?
GENERAL ORAL CONTRACEPTIVES

- FDA requirements for generic drug:
  - Drug concentration time curve with area under curve (AUC) and absorption rate
  - 90% CI for AUC values for generic may vary by -20% and +25%
  - Potency variation of +/- 10% between lots

The Contraception Report June 2002 Vol 13 #2
http://www.contraceptiononline.org
ORAL CONTRACEPTIVES

• Large intra- and interindividual variability in plasma steroid levels

• “With oral contraceptives, every woman makes her own individual cocktail on a day-by-day basis...Studies have shown that on two successive Mondays or two successive Tuesdays, you cannot predict the second pattern from the first pattern...Despite this, we still see contraceptive efficacy, which has never failed to amaze me.”

Joseph Goldzieher, M.D.
• Explanation to patients
  • Generics have not been shown to be effect (or ineffective) for preventing pregnancy
  • For some, reduced costs allow use of OCs
  • For others, the potential costs of unproven product may be excessive
  • ? Difference between 20 ug and >dose
QUICK START OCs

• Immediate start
• Direct observation of first pill
• Improved Compliance—continuation
• No reported increase in side effects

OCs and Weight Gain

• **Cochrane Review March 2003**
  - 3 placebo-controlled, randomized trials-- no evidence of a causal association between COCs or patch and weight gain.
  - Most comparisons of different COCs showed no substantial difference in weight.
  - “Available evidence is insufficient to determine the effect of combination contraceptives on weight, but no large effect is evident.”

“Birth control you only have to think about four times a year.”

‘The pill that lets you have just four periods a year’

Depo Provera,
Not Seasonale
DMPA

- Unscheduled bleeding common
- 50% amenorrhea at 1 year
- Weight gain—mean 2-3 kg/year
- Delayed return of fertility
  - No ultimate effect on fertility
- Now available in Sub-Q formulation
- Effect on bones
  - Osteopenia or failure of appropriate bone accretion
  - ?Reversible
Women who use Depo-Provera Contraceptive Injection may lose significant bone mineral density. Bone loss is greater with increasing duration of use and may not be completely reversible.

It is unknown if use of Depo-Provera Contraceptive Injection during adolescence or early adulthood, a critical period of bone accretion, will reduce peak bone mass and increase the risk of osteoporotic fracture in later life.

Depo-Provera Contraceptive Injection should be used as a long-term birth control method (e.g., longer than 2 years) only if other birth control methods are inadequate (see WARNINGS).

WARNINGS

• BMD should be evaluated when a woman needs to continue to use Depo-Provera Contraceptive injection long term.

• Other birth control methods should be considered in the risk/benefit analysis …in women with osteoporosis risk factors.
SAM POSITION PAPER
DMPA

- Likely low risk of fracture related to DMPA use
- Evidence of at least partial recovery after discontinuation
- Need to balance the physical, social, and economic cost of adolescent pregnancy vs the immediate and long-term impact of DMPA on bone
- Clinical Guidelines:
  - Continue to prescribe DMPA with counseling about risks and benefits in the adolescent population desiring DMPA use

Cromer, et al. JAH. 2006; 39: 296-301
CURRENT TRENDS IN CONTRACEPTION

- Developing new delivery systems
- Increasing access to full range of options
- Emphasizing successful use
- Widening use of emergency contraception
New Methods

- Single-rod Implant
- LNG IUS
- Sponge
- Vaginal Ring
- Monthly Injectable
- Patch
Transdermal Patch

- EVRA
  - Combination
    - Ethinyl estradiol 20 ug/d
    - Norelgestromin 150 ug/d
  - 7 days patch x 21 days; 7 days off
- Sites:
  - Abdomen
  - Arm
  - Buttock
  - Torso
### Distribution of Pregnancies by Baseline Body Weight Deciles (n=3319 subjects)

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<th>Decile Range (kg)</th>
<th>Weight Pregnancies</th>
<th>Total</th>
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<td>10</td>
<td>≥80</td>
<td>7</td>
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</table>

Etonogestrel/Ethynyl Estradiol
NuvaRing
Etonogestrel/Ethinyl Estradiol Vaginal Ring

- Progestin: Etonogestrel: 120 μg/day
- Estrogen: Ethinyl estradiol: 15 μg/day
- Worn for three out of four weeks
- Self insertion & removal
- Pregnancy rate 0.65 per 100 woman–years
- Approved October 2001

EXTENDED CYCLE—Beyond COCs

- Vaginal Ring
- Patch
- Data to support, but BTB still an issue
International Patterns of Contraceptive Use

Failure Rates: IUD vs Sterilization

5-Year Gross Cumulative Failure Rate

- LNG IUS
- CuT 380
- All sterilization
- Postpartum salpingectomy

Use of IUC by Female Ob/Gyns and by All Women in the United States

Why IUC is Underutilized in U.S.

- Dearth of trained and willing professionals to insert devices
- Negative publicity about method in early ’70s
- Misconceptions by health care providers and the public
- Fear of litigation

The 100 Worst Ideas of the Century

As a planet, we have celebrated almost every aspect of the 20th century. But let's face it, it wasn't all good. The past 100 years have seen plenty of dud inventions, foolish decisions and hugely embarrassing mistakes. Here's a list, not in any particular order, of 100 really bad calls. Wonderful thing, hindsight.

Which do you think was worst? Survey the list, then cast your vote!
Safety: Intrauterine Contraception
Copper IUDs Do Not Cause Infertility

- IUD not related to infertility
- Chlamydia WAS related to infertility

Nulligravid Women

<table>
<thead>
<tr>
<th>Presence of Chlamydia Antibodies</th>
<th>Odds Ratio for Tubal Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior Copper T IUD</td>
<td></td>
</tr>
<tr>
<td>1.0 (95% CI, 0.6 to 1.7)</td>
<td>1.0</td>
</tr>
<tr>
<td>2.4 (95% CI, 1.7 to 3.2)</td>
<td>2.4</td>
</tr>
</tbody>
</table>

IT’S NOT YOUR FATHER’S OLDSMOBILE
IT’S NOT YOUR MOTHER’S IUD
Dispelling Common Myths About IUC

• In fact:
  • CAN be used for nulliparous women
  • FDA approval for Cu-T IUD use in nulliparous women >= 16 yo
**Recent History of Intrauterine Contraception**

- **1988**: Copper T 380 IUD available in the US
- **2000**: LNG IUS available in the US

- Copper T 380A IUD
  - Copper ions
  - Approved for 10 years use

- LNG IUS
  - 20 mcg levonorgestrel/day
  - Approved for 5 years use
Levonorgestrel Intrauterine System (LNG-IUS)

- Overall failure rate 0.1 per 100 women
- Cumulative five-year failure rate is 0.7 per 100 women

Levonorgestrel 20 mcg/day
IMPACT ON BLEEDING

LNG IUS: Treatment Heavy Bleeding

MIRENA
Rates of Amenorrhea over 3 Years

0
1 0
2 0
3 0
4 0
5 0
6 0
7 0
8 0
9 0
1 0 0
3 6 9 1 2 2 4 3 6
The New Kid on the Block
poems by JACK PRELUTSKY

drawings by JAMES STEVENSON

IMPLANON
IMPLANON
# Features of Implants

<table>
<thead>
<tr>
<th></th>
<th>Implanon®</th>
<th>Norplant®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rod</td>
<td>Single</td>
<td>Six rod</td>
</tr>
<tr>
<td>System</td>
<td>Disposable applicator</td>
<td>Re-usable trocar</td>
</tr>
<tr>
<td>Length</td>
<td>4 cm</td>
<td>3.4 cm</td>
</tr>
<tr>
<td>Diameter</td>
<td>2 mm</td>
<td>2.4 mm</td>
</tr>
<tr>
<td>Carrier</td>
<td>Evantane®</td>
<td>Silastic®</td>
</tr>
<tr>
<td>Active Agent</td>
<td>68 mg etonogestrel</td>
<td>216 mg LNG</td>
</tr>
<tr>
<td>Duration of Use</td>
<td>3 years</td>
<td>5 years</td>
</tr>
</tbody>
</table>
Contraceptive Efficacy

- Clinical Trials: No pregnancies during 1200 woman-years of exposure (Pearl Index, 0; 95% CI 0.0-0.2)
- FDA Definition of Pregnancy: 6 pregnancies/20,648 cycles (Pearl Index, 0.38/100 woman years)
- Effective contraception that lasts for 3 years
- Effectiveness not studied in women 130% IBW

Approved July 2006

OTHER METHODS

• Barriers
  • New male condoms
  • The sponge
  • Vaginal microbicides +/- spermicides
  • Female condoms
  • Diaphragm
  • Cervical Cap
BELT AND SUSPENDERS
eZ-on Male Condom

- Polyurethane Film—Not Latex (allergies)
- Baggy and unrolls either direction
- Randomized, controlled crossover trial of clinical acceptability
  - 345 couples, 2624 uses
  - Did not perform as well as standard latex
    - Clinical breakage rate 6% vs 1%
    - Slippage 2% vs 1%
    - Overall “failure rate” 7% vs 2%
  - Preferences evenly split
    - ~30% preferred the new condom
- Currently available
The Sponge

- Today sponge
- Off the market since 1995; IT’S BACK
- Manufacturing problems
- Approved by FDA April 2005
- New company—Allendale pharmaceuticals
- Available in Pharmacies
- “One size fits all”
- Failure rate:
  - typical parous users 28 pregnancies/100 women years
  - Typical nulliparous: 18 pregnancies/100 women years
Vaginal Spermicides/Microbicides

- Failure rate 28.2%--typical users; rate corrected for under-reporting of Abs
  (Fu et al. Fam Plann Persp 1999;31(2):56-63)
- Motivation for development from STD/HIV perspective
  - +/- spermicidal properties of microbicides
- Active area of research
- Effect on vaginal ecosystem
  - Microbiology
  - Colposcopic assessment of abrasions/lesions
Dual Method Efficacy

- Perfect use of male condoms 3%
- Perfect use of spermicide 6%
- Perfect use of both together 0.1% **

** as good as OCs . . .

Contraceptive Technology, 1998
Female Controlled Barriers

- Female Condom
  - Reality®
  - Several Models available outside U.S.
  - Variable acceptability by population
  - Use for STD risk primarily, contraception secondarily
AND FINALLY
THE EVENING AFTER
THE DAY FOLLOWING
THE MORNING AFTER
THE NIGHT BEFORE
PILL

Emergency contraception isn't just for the morning after - it can be started up to 3 days (72 hours) after unprotected sex. Emergency contraception is free and confidential - ask your doctor or family planning advisor for further information.

EMERGENCY CONTRACEPTION
IF LAST NIGHT WENT WITH A BANG

YOU'VE GOT 3 DAYS TO DEFUSE THE SITUATION

Emergency contraception isn’t just for the morning after - it can be started up to 3 days (72 hours) after unprotected sex. Emergency contraception is free and confidential - ask your doctor or family planning advisor for further information.
After you've got it together

You've got 3 days to get it together

Emergency contraception isn't just for the morning after - it can be started up to 3 days (72 hours) after unprotected sex. Emergency contraception is free and confidential - ask your doctor or family planning advisor for further information.

Emergency contraception
IF YOU'VE BEEN SWEPT OFF YOUR FEET

YOU'VE GOT 3 DAYS TO GET THEM BACK ON THE GROUND

Emergency contraception isn’t just for the morning after - it can be started up to 3 days (72 hours) after unprotected sex. Emergency contraception is free and confidential - ask your doctor or family planning advisor for further information.
EMERGENCY CONTRACEPTION

USE WITHIN 3 DAYS OF OPENING

Emergency contraception isn’t just for the morning after - it can be started up to 3 days (92 hours) after unprotected sex. Emergency contraception is free and confidential - ask your doctor or family planning advisor for further information.
As long as:

- Condoms break
- Inclination and opportunity unexpectedly converge
- Diaphragms and cervical caps get dislodged
- Women are raped
- People are so uncomfortable about sex that they need to feel swept away
- IUDs fall out.

We will need morning-after birth control. Our birth control technology is imperfect, and the human psyche is imperfect. Family planners who don't offer postcoital contraception shortchange their patients.

Hatcher et al. Contraceptive Technology, 1984
24-hour EMERGENCY HOTLINE:
1-888-NOT-2-LATE

http://opr.princeton.edu/ec/
EMERGENCY CONTRACEPTION

• Mini-pills (Progestin only—Plan B)
  • [http://www.go2planb.com](http://www.go2planb.com)
• Combination OCs (Yuzpe regimen—Preven no longer manufactured)
• Cu-T insertion
• Other anti-progesterones
Progestin-only ECP
Effectiveness: Single Use

100 women have unprotected sex in the 2nd or 3rd week of their cycle

8 will become pregnant without emergency contraception

1 will become pregnant using progestin ECPs (88% reduction)

Source: WHO 1998
EMERGENCY CONTRACEPTIVE PILLS
Reduction in Unintended Pregnancies

Pregnancies prevented by ECPs

- Use ECPs: 75% effective
- Pregs among non-users: 3.2 million
- Use ECPs: 2.3 million

Use ECPs to prevent unintended pregnancies.
EMERGENCY CONTRACEPTIVE PILLS
Reduction in Abortions
Abortions prevented by ECPs

- Abortions
- Pregs among non-users
- 75% use if cont. failure

Use ECPs-75% effective

Million Abortions

0.5
1
1.5

1.4
1

0

Pregs among non-users
75% use if cont. failure
EMERGENCY CONTRACEPTION

• CW—take anytime within 72 h

• Dosing
  • ASAP—LNG or Yuzpe
    • The Lancet 1999. 353:721
  • Single dose
    • 1.5mg Lng vs 2 doses 0.75mg Lng vs 10 mg Mifepristone--Von Hertzen et al. Lancet 2002; 360: 1803-10
    • Up to 120 hours

• Copper IUD
EMERGENCY CONTRACEPTION: Mechanism of Action of Plan B

- Decreases the number of sperm that can be recovered from the uterine cavity by 3 hours after ingestion; by 5 hours, immobilizes sperm; by 9 hours, thickens cervical mucus
- Ovulation suppression
  - Plan B taken prior to LH surge, suppresses surge and ovulation
  - Plan B taken closer to LH surge, blunts the surge
- No increased risk of ectopic pregnancy; therefore, likely does not slow or prevent normal movement of fertilized ova through Fallopian tubes
- Decreased levels of Progesterone in luteal phase, explaining early bleeding after Plan B, but this may be due to inhibition of LH surge
- When taken after fertilization, recent studies show lower effectiveness-- contrary expected result if interference with implantation
- Delay in use of Plan B causes decreased effectiveness; If Plan B interfered with implantation, its efficacy should not decrease with delay in use as long as it is taken before implantation

PLAN B: Informed Consent and Evidence

- Personal decisions about moral acceptability should be respected
  - Package labeling indicates that its use may affect postfertilization events

- Women should be informed of the evidence:
  - that the ability of Plan B to interfere with implantation remains speculative, with virtually no evidence supporting that mechanism and some evidence contradicting it

- Women should be informed of the best available evidence:
  - Plan B’s ability to prevent pregnancy can be fully accounted for by mechanisms that do not involve interference with postfertilization events

Davidoff, F and Trussell, J. Plan B and the Politics of Doubt. JAMA Oct 11, 2006;296 1775-7
Availability of levonorgestrel preparations for emergency contraception (as of November 2002)
Definition of Pregnancy

• NIH/FDA
  • Pregnancy encompasses the period of time from confirmation of implantation until expulsion or extraction of the fetus.

• ACOG
  • Pregnancy is the state of a female after conception and until termination of the gestation. Conception is the implantation of the blastocyst. It is not synonymous with fertilization; it is synonymous with implantation.

Source: US Government 1983; Hughes 1972
**ECPs OTC**

- Application to FDA regarding OTC status
  - Available OTC in >30 countries and 5 states
  - Support from >80 medical organizations
  - Two FDA Advisory Committees recommended approval
  - FDA Staff recommended approval
  - Application denied May 2004
  - Decision postponed September 2005
“Politics Trumps Science”

- The argument: greater availability would increase risky sexual practices among teens
- The evidence: Nil, and to the contrary
- Analogous to suggesting that a “fire extinguisher beneath the kitchen sink makes one a risky cook”—Grimes
- NEJM Editorial .”. .”…the FDA’s decision-making process is being influenced by political considerations”
ECPs OTC—Current Status

• August 24, 2006 OTC sale approved by FDA for individuals >=18 years old
  • Proof of age required with ID
  • Only available in pharmacies staffed by a licensed pharmacist
    • Not sold at gas stations or convenience stores

• Remains available by prescription for those 17 and younger

• Advance prescription recommended by national organizations

• State initiatives to allow pharmacy provision/prescription by pharmacists -- Collaborative Practice States
  • Alaska, California, Hawaii, Maine, Massachusetts, New Mexico, New Hampshire, Vermont, Washington
ECPs OTC—Current ISSUES

• Pricing
  • Current Prescription Pricing: $25-$40
  • Clinics with sliding scale pricing—Planned Parenthood
  • Most OTC products are not covered by insurance
  • Medicaid does not cover OTC drugs
  • States can use state funds to cover Plan B
    • California and Minnesota will cover
  • Federally-funded health centers may offer discounts under the 340B Drug Discount Program and pass along savings
  • Lawsuit against the FDA by the Center for Reproductive Rights—could result in lifting of age restrictions
UNINTENDED PREGNANCY
FOR MORE INFORMATION:

• http://www.contraceptiononline.org

• http://www.arhp.org
Testosterone undecanoate (Phase III trial)
Suppression of spermatogenesis: TU versus TU + DMPA

**Suppression** (24 weeks)
**Maintenance** (24 weeks)
**Recovery**

Weeks follow up

Spam concentration (million/mL)