

# Contraceptive Technology

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## Norplant Contraceptive System

### I. Description of System

- A. 6 silastic, soft, flexible capsules, 34 mm long x 24 mm in diameter, loaded with 36 mg levonorgestrel, which is slowly released:
  - 1. 80 mcg/d at first
  - 2. 34 mcg/d after 2-6 months
  - 3. 25 mcg/d at 60 months
- B. Number of capsules dictated by surface area to volume ratio required for stated serum levels
- C. Capsules are nonbiodegradable

### II. Benefits of Norplant Contraceptive System

- A. Achieves excellent contraceptive effect with very low, consistent dose of steroid hormone. Side effects for hormonal therapies are generally dose-related
- B. Long lasting
  - 1. Up to 5 years
  - 2. 6th year pregnancy rate is roughly equivalent to OC failure rate
- C. Low motivational method: once inserted, no further compliance efforts are needed
- D. Rapid onset: protection starts in 24 hours
- E. Rapidly reversible: first cycle fertility is normal (18% pregnancy rate)
- F. High level of continuation rates
  - 1. 90% first year
  - 2. 29.5% for full 5 years
  - 3. 75 % of those requested 2nd set

### III. Failure Rates With Norplant

- A. Overall
  - 1. First year failure rates: 0.2%
  - 2. Cumulative 5-year failure rates: 3.9%
- C. Only 'soft' capsules are marketed in the United States. There is no increase in failure rates for heavier patients (>70 kg) who had 5-year cumulative failure rate of 1.1%

### IV. Other Pregnancy-related Questions

- A. Ectopic risk
  - 1. Absolute risk decreased
    - a. 1.3/1000 woman yrs--Norplant Contraceptive System
    - b. 2.7-3.0/1000 woman years---no method of birth control
  - 2. Ratio of extrauterine/intrauterine pregnancies is higher. Up to 20% of pregnancies can be ectopic. Norplant is more

We are not really just talking about contraception, we are talking about sexuality. We are talking about women that are going to have sexual intercourse. So we have to have a realistic view of contraception and know that what we are trying to do is make having sexual intercourse a fun, safe activity for our patients. Women are at risk for having an unwanted sexually transmitted disease, that is pregnancy if they don't want to get pregnant, or other unwanted sexually transmitted diseases which are the whole litany that you have probably heard about at some point.

Another thing about contraception is that there is a lot of bad information out there. Very few are actually getting their contraceptive information from their physician. You know the boyfriend is just going to say, "Ah. Don't worry about it." You know that the media is only going to dramatize the negative aspects. How many news articles or articles in women's journals have you read that list all the non-contraceptive health benefits of oral contraceptives? None. They all tell about the major risk factors of contraceptives.

effective at preventing intrauterine pregnancies.

**B. Teratogenicity**

1. The concern would be that the androgenic progestin (levonorgestrel) might cause masculinization of female infants. However, the only reported congenital anomaly was a male infant born with ambiguous genitalia.
2. Decades of experience with norgestrel and levonorgestrel in oral contraceptives (OCs) at much higher doses are reassuring. Older concerns with limb reduction, hypospadias, and cardiac anomalies have been disproved.

**C. Breast feeding**

1. Package labeling information recommends waiting until 6 weeks postpartum to insert Norplant. However, this is not consistent with other progestin-only methods. Progestins do not interfere with prolactin or any other aspect of milk production.
2. Growth parameters of infants exclusively breast fed by Norplant users were followed until child reached age. Growth of these children was completely normal.

**V. Menstrual Cycle Changes**

- A. Every woman will experience change in menses; 80% note changes. Initially, 3 distinct patterns emerge with roughly equal frequency
1. Amenorrhea
  2. Subtle cycle length and/or cycle flow changes
  3. Spotting and bleeding
- B. Amenorrhea, spotting, and bleeding usually resolve within 3-6 months, but 10-20% of women in clinical trials still experienced some of these problems at 4 years
- C. Precounseling and screening are vitally important to patient satisfaction and method continuation
1. Amenorrhea
    - a. Pregnancy concerns
    - b. Patient's general health concerns
  2. Bleeding and spotting
    - a. Not medically significant (hemoglobin usually stable)
    - b. May cause significant life style issues
      - (1) Active women
      - (2) Women who wear scant undergarments
      - (3) Women in relationships where intercourse is prohibited if there is any bleeding
  3. Up to 40% of women request removal in the first year in the absence of personal preinsertion counseling, compared to 10% when preinsertion counseling is done

- D. Management recommendations for spotting/bleeding
1. If patient will tolerate, allow 3-6 months to resolve spontaneously
  2. If persistent or worsening spotting/bleeding
    - a. Rule out other etiologies
    - b. Treat according to underlying cause
      - (1) Continuous daily spotting due to atrophic endometrium
        - (a) Recommend trial of ibuprofen 20-400 mg po q4-6h 5 days at end of menstrual flow each affected cycle (research recommends 800 mg tid for 5 days)
        - (b) If that is not successful, skip (2) below
      - (2) Intermittent spotting due to endogenous estrogen production swings
        - (a) Recommend ethinyl estradiol 0.02-0.05 mg qd each day of affected cycles, starting at end of menses
        - (b) Use estrogenic OC for 1-2 months until levonorgestrel levels fall
        - (c) Conjugated equine supplements usually produce subtherapeutic estrogen levels, but they are occasionally effective
        - (d) If patient is deeply troubled, remove capsules

## VI. Metabolic Effects

- A. Glucose tolerance. Clinical trials show slight increase in 1-hour value of glucose tolerance test. Not contraindicated in diabetics with no renal or vascular compromise. The incision should be watched for possible infection.
- B. Lipid profiles
  1. Total cholesterol falls, and HDL levels may fall
  2. LDL drops for 3-6 months, but returns to baseline
  3. Essentially neutral effect on lipids
  4. Not contraindicated in patients with lipid abnormalities
- C. Coagulation impacts/disorders
  1. No estrogen in Norplant. No consistent pattern of factor changes seen during clinical trials.
  2. Only active thrombotic disease prohibits Norplant use. Patients with history of DVT or PE are candidates for Norplant.
  3. In anti-coagulated patients, reverse anticoagulants before insertion or removal to prevent hematoma formation.

## VII. Other Side Effects

- A. Weight changes: gain (54%); loss (32%)

- B. Acne, depression, breast tenderness, headache, hair loss, varicosities, nausea, vomiting, vaginitis, mood swings, etc.
- C. Suggestion: administer progestin-only pill for appropriate trial period in Norplant candidates who have histories of complications which caused them to discontinue OCs, such as nausea, vomiting, bloating, hypertension, to determine if side effect was estrogen- or progestin-related
- D. Note: Trial with progestin-only pill or DMPA does not reliably predict bleeding or other problems with Norplant

### **VIII. Contraindications to Use of Norplant Contraceptive System**

- A. Known or suspected pregnancy
- B. Active thrombophlebitis or thrombotic disorders
- C. Undiagnosed abnormal genital bleeding
- D. Acute liver disease; liver tumors
- E. Known or suspected breast cancer
- F. Coronary artery or cerebrovascular disease
- G. Medical problems aggravated by fluid retention (strong relative contraindication)
- H. Concomitant use of rifampin or anticonvulsants such as phenytoin, phenobarbital or carbamazepine (strong relative contraindication)
- I. Note: Norplant is not contraindicated in women with:
  1. Previous DVTs or PEs
  2. Smokers >35
  3. Diabetes
  4. Systemic lupus erythematosus
- J. Note: Norplant is not an excellent choice for severely handicapped or retarded patients who would have hygiene problems with prolonged spotting or bleeding or who might not be able to cooperate with insertion and removal procedures

### **IX. Mechanisms of Action of Norplant Contraceptive System**

- A. Ovulation suppression important in years 1-2
  1. Only 10-18 % of cycle showed ovulatory progestin levels in early years. Up to 60 % of women ovulate in later years
  2. FSH, LH, and progestin levels suppressed
  3. Estrogen levels are maintained at or above follicular phase levels, so there is no concern about estrogen deficiency with Norplant use
- B. Cervical mucus hostile to sperm penetration (most important mechanism)
- C. Atrophic endometrial lining
- D. Inadequate luteal phase appears in ovulating patients

### **X. Management of Serious Complications with Norplant**

- A. Cellulitis after insertion--antibiotic therapy
- B. Abscess after insertion---remove Norplant and incise and drain abscess
- C. Expulsion of capsule---insert new capsule
- D. Jaundice---remove Norplant
- E. Severe depression--remove Norplant
- F. Visual changes in contact lens users--refer to ophthalmologist

## XI. Implant Removal Techniques and Tips

- A. Palpable implants before removal
  - 1. Standard technique: straight forceps creating plane under implant. Curved forceps grasp at 90° angle and deliver from incision. Fibrous capsule dissected away from tip. Norplant implant removed
  - 2. Pop-out technique: manipulate tips to central point
  - 3. Infuse minimal anesthetic over tip. Make minimal incision and manually maneuver each implant through incision
  - 4. U-technique: performed with modified no-scalpel vasectomy clamps, incision parallel to implants. Grasp unit one-third of way from tip. Raise and evert, creating U-shape. Dissect fibrous capsule away and remove implant
- B. Palpable implants: tips to enhance visibility
  - 1. Mark on skin with skin marker prior to removal
  - 2. Betadine swab technique
- C. Nonpalpable implants
  - 1. Implants are radio-opaque
    - a. Careful positioning for x-ray study vital. Have x-ray technician put marker over insertion scar to aid in localizing at time of removal
    - b. Cross table and lateral films helpful for making certain implants are above fascial plane
  - 2. Ultrasound visualization
    - a. Need high frequency machine able to image superficial structure
    - b. Modify OB ultrasound by putting a pillow of ultrasound contact gel on arm
    - c. Can do removal with real-time ultrasonic guidance

## Injectable Progestins--Depo-medroxyprogesterone Acetate (DMPA)

### I. Efficacy

- A. Failure rate first year: 0-0.32 (life table analysis)
- B. Cumulative 3-year failure rate: 0.75 (life table analysis)
- C. Pearl index (pregnancy rates/100 women years):
  - 1. Year 1:0.3

If we look at our various forms of reversible contraception in the United States, what we see here are the failure rates for oral contraceptives, IUDs, Norplant, Depo-Provera are very high. We don't see the same kind of use failure with IUDs or with the other methods. The use failure rate for IUDs is the pregnancy rate associated with someone that has expelled their IUD but doesn't realize it.

ParaGard IUD has come out and once the idea of a long acting form of contraception that you don't have to think about was promoted in the contraceptive market place, ParaGard started to pick up a significant number of patients. Since the ParaGard has been introduced into the United States in the late '80s, there have been no physician or company related malpractice suits directed at the IUD, so it is very safe. Our patient spectrum is very narrow but we aren't seeing the same litigious nature that was around that got the removal of all the other IUDs except for the Progestasert from the market.

There are new cervical caps that are on the market. We have new condoms, not only male condoms but the female condoms. We are seeing that there might be a significant number of patients that have a latex sensitivity, not a true latex allergy, and there are new non-latex condoms that are coming out and again the female condom. We have new progesterones in our oral contraceptives and the new big kid on the block is Depo-Provera.

We also have a wider range of choices. You can't catalog a patient and just say that all you are going to use is oral contraceptives because they have a high success rate and they have these non-contraceptive benefits. They have low user motivation because we know there are a lot of women that are out there that don't like to be on oral contraceptives. A patient who is experimenting with sexual partners needs to have a very high success rate for contraception but also wants to avoid unwanted sexually transmitted diseases. So you need to use two methods. One is protecting against STDs and the other one is to protect against unwanted pregnancies. Since there isn't a method that does both to the highest degree, use two methods.

We have new applications for oral contraceptives. We have the low dose pill for our mature gravidas. We have new low-dose pills. The concept is that women can take some form of hormone from the second they start having periods until they die. We have the standard oral contraceptives and then we have this new low dose pill that has 20 micrograms of ethinyl estradiol and 0.5 mg of norethindrone and then we just segue right into hormone replacement therapy and then the patient dies. So the pharmaceutical companies can attack our patients at every age group with some form of hormones.

Medical diseases that used to be contraindications to oral contraceptive use really are either just relative contraindications or actually will be benefitted by using oral contraceptives. There has been a lot of press recently about this new form of contraception that can be used when a method fails or after if someone has had unprotected intercourse.

Condoms have a high favorability rating and the IUD has a low favorability rating. But when you talk to the individual user, what you see is that some of these methods like the IUD, the foam, pill here, again, sterilization, for the individual user have a very high user favorability rating.

Another thing is that we have to remember that our younger age patients and our mature patients are the ones that need contraception the most because those are the group that don't think they are going to get pregnant. You take somebody under the age of 20. We know that teenagers are sexually active for at least 6 months before they come into a health care providers office and start asking about contraception. There is a lot of risk-taking behavior in this group because teenagers don't think they are going to die, don't think they are going to get sick, don't think they are going to get pregnant. Once women get over the age of 40, normal fecundity starts dropping and maybe the woman is starting to have some irregular periods. This group, too, is the one that stops using their contraceptive method and runs the greatest risk of pregnancies.

Only half of unintended pregnancies are in patients that are using contraception. This is user failures to make sure that if somebody is using a form of contraception. Unwanted pregnancies, i.e. abortion, are the highest in the mature group and the teenage group. So if we want to have an impact on unwanted pregnancies, these are the groups to target. Discuss with them when they walk through the door what form of contraception they want.

Oral contraceptives. Most of the oral contraceptive efficacy was because of its progesterone effect. Estrogen was actually added in the original oral contraceptives as a contaminant. The original idea behind oral contraceptives was to give

2. Year 2:0.1
3. Year 3:0.4
4. Year 4:0.1
5. Year 5:0.0
6. Cumulative (5 years): 0.9

## II. Side Effects

### A. Menstrual changes

1. Virtually every woman will experience changes (some women experience more than 1 change)

#### Percent of Patients Experiencing Changes in Month

<u>Change</u>	<u>3</u>	<u>6</u>	<u>9</u>	<u>12</u>
No change	12.1	7.7	5.4	1.9
Amenorrhea	8.3	22.0	38.5	44.6
Infrequent	57.3	50.6	42.7	36.9
Frequent	5.7	4.1	4.1	5.4
Irregular	15.9	15.0	9.2	10.8
Prolonged	28.7	17.8	10.8	9.9

2. Days of post-injection bleeding in percent of patients

<u>Months after injection</u>	<u>0 days</u>	<u>1-7 days</u>	<u>8-10</u>	<u>11-30</u>
				<u>days</u>
3	29.3	28.0	10.2	32.5
6	39.0	28.5	9.3	23.1
12	54.6	25.9	7.1	12.4
36	73.8	17.5	3.6	5.1

3. Overall trends with increasing duration

- a. Amenorrhea increases
- b. Number of bleeding episodes decreases
- c. Length of bleeding episodes decreases

### B. Frequent medical side effects (occurring in > 1% of subjects)

Headaches	17.5 %	Edema	2.2 %
Abdominal discomfort	11.9 %	Back pain	2.2 %
Nervousness	11.6 %	Dysmenorrhea	1.8 %
Dizziness	5.9 %	Depression	1.6 %
Loss or decreased libido	5.8%	Aches	1.29
Fatigue	4.5 %	Pruritus	1.2 %
Limb/varicose vein pain	3.9%	Alopecia	1.2%
Nausea	3.5 %	Rash	1.1%

## III. Metabolic Impacts

### A. Lipids

1. Versus controls
  - a. Cholesterol, triglycerides, HDL: decrease

the patients a progesterone only pill. What they found is that when it was contaminated with mestranol, the patient had less unwanted breakthrough bleeding. So, oral contraceptives began with 80-150 micrograms of ethinyl estradiol. Then they started to look at what is the lowest level of ethinyl estradiol compared to the standard level of progesterone that would decrease breakthrough bleeding. 80 micrograms of ethinyl estradiol, nobody had breakthrough bleeding and at 20 micrograms of ethinyl estradiol, 50% of patients had breakthrough bleeding and at 30 micrograms of ethinyl estradiol, the percentage of breakthrough bleeding dropped down. At 30 micrograms it is about 20% and at 50 micrograms it is around 10% but you will always have some degree of breakthrough bleeding. Any large contraceptive study is going to show that the risk of breakthrough bleeding with the newer formulations of oral contraceptives is anywhere from 10-25%.

The advantages of oral contraceptives is that they are very effective and they are easy to use. The disadvantages is these are synthetic agents so we can't use a natural compound. The progestins are all some derivative of testosterone. The estrogens are now exclusively ethinyl estradiol. The potency varies because it's got to be converted to its active form and that conversion varies from patient to patient. Take three women, give them the exact same oral contraceptive, the exact dose, taken it the exact same way, they are going to have three different degrees of side effects because how they metabolize these synthetic agents differently.

Mechanism of action. Progesterone inhibits the gonadotropin surge. You change the cervical mucus to decrease sperm penetration, you change tubal motility. Therefore, the sperm, the egg or the fertilized oocyte does not get transported to the endometrium in time. We decrease the endometrial glycan production so that we don't have enough energy for the blastocyst. It acts as an abortifacient. You can tailor it any way you want to but that is basically what all forms of contraception are to a greater or lesser extent. Hormonally active contraception.

The estrin effects. Nausea. Breast tenderness. Fluid retention. Changes in circulating vitamin levels. An increase in angiotensin so a potential increase in blood pressure. We know that the hepatic production of globulins is changed and we also might see some mood changes.

Our pure progestational contraceptive methods have the greatest impact. When we talk about Depo and we talk about Norplant, we will see that one of the biggest reasons for patients discontinuing both of those methods of contraception is weight gain. We change our estrin receptors around the endometrium so it is protective of the endometrium. We have some effect on our HDL/LDL profile. This also depends on the potency. Some of the levonorgestrel containing preparations have a slightly greater impact on the HDL/LDL profile and it relates to the amount.

There are some serious side effects due to oral contraceptive use. You can increase the risk of gallstones. You can see heart attacks. You can see blood clots and thromboembolic events. You can see strokes, liver adenomas and hypertension. This is the relative risk. You can see that these effects, particularly in your smokers over the age of 35, are really fairly minimal.

There are certain things that are associated with oral contraceptive use. Contraceptives, that is all they will hear for the rest of the day.

The data shows that there might be a 1.1% relative risk of breast cancer. It might be associated with the earlier use of oral contraceptives. Some studies show a slightly increased risk, other studies show a slightly decreased risk.

The liver cancer melanomas are not increased. Cervical dysplasia is increased but a lot of these studies have many confounding variables. A woman that is on oral contraceptives gets more visits to her obstetrician, gynecologist or health care provider. She has more chance of having a pap smear. She might have more sexual activity. Therefore, we might see more dysplasia but there is no data on an increased risk of cervical cancer and we know that for all comers, there is a 50% decrease in endometrial cancer. It lasts for up to 15 years after the oral contraceptives have stopped.

For every age group, oral contraceptive use and smoking is not good. It goes up after the age of 35 and significantly rises after the age of 45. Document in your medical record that you gave her all this information. If she wants to continue to smoke and she understands what the risks are and it is documented.

The positive effects. There is a 40% reduction in ovarian cancer in every use of oral contraception. If a patient is on oral contraceptives for more than 10 years, this is 80% reduction in the risk of ovarian cancer. Don't promote oral contraceptives as a method of decreasing one of the most silent and deadly forms of gynecologic cancer. Another form of cancer reduction is endometrial cancer.

- b. LDL: no change or increases
- 2. Prospective, noncomparative
  - a. Cholesterol, triglycerides, HDL: no change or decrease
  - b. LDL: no change or increases
- 3. Prospective, comparative
  - a. Cholesterol, triglycerides, HDL: no change
  - b. LDL: no change
- B. Glucose tolerance
  - 1. Patients with normal glucose tolerance: glucose and insulin levels increase, but usually remain in normal range
  - 2. Concern: patients with history of impaired tolerance may develop impaired glucose tolerance or overt diabetes
  - 3. Overt diabetics may have increased glucose levels, but rarely need change in insulin therapy
- C. Hemoglobin
  - 1. Mean levels stayed within normal range and increased over time
    - a. Initial hematocrit: 13.1
    - b. 12 month Hematocrit: 13.6
    - c. 24 month Hot: 14.0
  - 2. Incidence of anemia decreases with duration of use
- D. Coagulation
  - 1. Increased risk for thrombophlebitis noted over expected value
  - 2. No increase in DVT or PE
- E. Blood pressure
  - 1. No induction of hepatic protein synthesis
  - 2. Clinical trials show overall decrease in both systolic and diastolic pressures
  - 3. Some idiosyncratic increases
  - 4. Hypertension not contraindication
- F. Impacts on estrogen-sensitive systems
  - 1. Estrogen levels within normal early follicular phase range for ovulatory women. Some fall below those levels
  - 2. Bone metabolism
    - a. Animal data (10-year monkey study)
      - (1) Bone loss proportional to DMPA dose (up to 50 times therapeutic dose tested)
      - (2) At contraceptive doses, x-rays showed no bone density changes
    - b. New Zealand study found increased risk of osteoporosis with DMPA use
      - (1) Problem: cross-sectional study. Pretreatment tests not available for patients. No loss seen in

Non-contraceptive health benefits from oral contraceptives. The estrogen decreases cardiovascular disease. It has a positive effect on the HDL/LDL profile. Progestin effect. Decreased pelvic inflammatory disease by thickening the cervical mucus. Those offending agents can't get up into the upper tract. Endometriosis is decreased because of the progestational effect on decreasing estrin receptors, increasing the breakdown of estrogen and therefore there is no estrogen to stimulate the endometrial implants. Decreased uterine fibroids.

Because of the progesterone dominant effect of oral contraceptives, this actually might decrease the effect of fibroids. Because fibroids concentrate estrogen receptors and possibly one of the reasons why they grow is because they have a locally rich environment of estrogen. You put estrogen and progesterone together you get less ovarian cysts, you get less ectopic pregnancies. Less benign breast disease. Less rheumatoid arthritis. Less menorrhagia. Less dysmenorrhea. Less iron deficiency anemia.

We know that there are certain contraindications. Cholestatic jaundice of pregnancy. Hepatic adenomas. Current rifampin use. Women who smoke who are over at that magical age and malabsorption syndrome. Thrombophlebitis or thromboembolic disease. You might not want to put an IUD in that patient because of the bleeding associated with IUD. You might not want to use something that will have higher risk of abnormal and irregular menses like progesterone only contraceptive agents. So you can use oral contraceptives while a patient is on their Coumadin and then once they stop their Coumadin after six months, then you should take the patient off of their oral contraceptives.

Women over the age of 40. We know that there are some newer lower dose preparations that are coming on the market. The 20 microgram pills. The very low dose progesterone pills. These are, a nice segue between oral contraceptive use and hormone replacement therapy.

If somebody is not greater than 30% over the ideal body weight, they have a normal glucose screen, there is no family history or risk of coronary artery disease before the age of 50, negative mammogram, normal lipid profile, you can use oral contraceptives in that age group. For someone that has had a contraceptive failure, barrier failure or just did not use a form of contraception, we can use interception. The best is Ovral but any of the higher dose pills will work. The patient will take two tablets when they are at risk and then two tablets 12 hours later. They do have a lot of side effects from this such as nausea and the high estrogen-progesterone effect of taking that many tablets in a short period of time. There is a 2% failure rate and the failure rate goes up if it is not initiated in a 48-72 hour time frame.

DMPA users during study

(2) Some women gain bone mass after stopping DMPA

- c. Postmenopausal women on DMPA show higher bone mass than non-users
- d. Postmarketing study planned. Might consider impact on slender, smoking patient with family history of osteoporosis (high-risk patient)

#### IV. Weight changes

- A. Majority of patients gained weight
  - 1. 60% had weight gain after 6 months
  - 2. 75% had weight gain after 24 months
  - 3. 85% had weight gain after 5 years
- B. Amount of weight gain: 2 pounds in first year
  - 1. One study demonstrated 7.5 kg gain after 6 years
  - 2. Most studies have not had control group for comparison

#### V. Continuation/discontinuation Rates

- A. Continuation rate at end of 1 year: 51.1%
- B. Discontinuation rate at end of 1 year: 38.9%
  - 1. Lost to follow-up: 4.0%
  - 2. Medical reason: 3.5%
  - 3. Nonmedical reason: 9.3%
  - 4. Amenorrhea: 10.3%
  - 5. Heavier bleeding: 0.9%
  - 6. Longer bleeding: 6.5%
  - 7. Irregular bleeding: 4.2%

#### VI. Return to Fertility

- A. Time from last injection to conception
  - 1. Range: 4-24 months
  - 2. Median: 9-10 months
    - a. <6 months: 9.6%
    - b. <12 months: 67.0%
    - c. <18 months: 93.3%
    - d. <24 months: 97.1%
- B. Not related to number of injections
- C. Time to conception proportional to body weight at the time of last injection

#### VII. Teratogenicity Concerns

- A. No increased risk of birth defects with in utero exposure
- B. Israel study of long-term follow-up: no differences found
- C. Thailand study: risk of low birth weight and infant death increased within 4 weeks of injection
  - 1. Early, high-dose in utero exposures to DMPA may affect

fetal growth and survival

2. Long-term follow-up showed growth after birth same as general population

### **VIII. Mechanisms of action**

- A. Inhibits ovulation
  1. FSH and LH levels suppressed
  2. No LH surge
- B. Pituitary remains responsive to GNRH
- C. Endometrium shallow and atrophic
- D. Cervical mucus thickens. Sperm penetration limited
- E. Fallopian tube motility decreases

### **IX. Pharmacokinetics**

- A. No accumulation of drug with repeated injections
- B. No correlation between body mass and plasma concentrations
- C. No correlation between body mass and time to reach undetectable plasma levels
- D. Drug rapidly metabolized once in bloodstream; absorption rate determines long action

### **X. Patient Management Issues**

- A. Start
  1. Office visit, examination, and informed choice
  2. First injection within 5 days of LMP
    - a. Give 150 mg in upper outer aspect of gluteal muscle or deltoid
    - b. Do not massage injection site.
- B. Continuation
  1. Give additional 150 nag IM injection every 3 months
  2. If interval >14 weeks, injection appropriate if sensitive pregnancy test is negative (especially if cervical mucus is thick)

## **Female Sterilization**

### **I. Recent trends in sterilization**

- A. Sterilization is the most common method of contraception in the United States for married women over age 30
  1. More than 25 million women have undergone sterilization since 1970
  2. In 1987, 640,000 women were sterilized
  3. Most sterilizations are now performed postpartum
    - a. In 1970, 1 woman in 25 who gave birth had postpartum sterilization
    - b. By 1985, 1 in 10 was given postpartum tubal sterilization

- B. Relative increase in female voluntary sterilization
  1. In 1972, 37% of procedures performed on women
  2. By 1987, the percentage had risen to 66%
- C. Laparoscopy revolutionized female sterilization and enabled simpler and safer techniques with virtually no sacrifice in efficacy
- D. Trials of outpatient surgery performed under local anesthesia were encouraging
- E. Cul-de-sac approaches to tubal procedures have been largely abandoned due to unacceptably high infection rates and availability of transabdominal laparoscopic methods

## II. Methods

- A. 1988 AAGL survey showed:
  1. 54% of procedures used bipolar electrosurgery
  2. 10% used unipolar electrosurgery
  3. 25% used silastic band
  4. 11% used spring clip
- B. Laparotomy procedures
  1. Usually done concomitantly with cesarean section or with another surgical procedure
  2. Pomeroy technique
    - a. Partial salpingectomy in which a loop of fallopian tube is ligated with rapidly absorbable suture material and transected
    - b. Important not to crush tube prior to ligation, since this increases fistula formation
    - c. Failure rates
      - (1) 1/200 in postpregnancy states
      - (2) 1/300 in interval method
  3. Irving technique
    - a. Only done in conjunction with cesarean section
    - b. The proximal stump is buried in myometrium and distal portion is tucked into the leaves of the broad ligament
    - c. Failure rates are minimal
  4. Uchida technique
    - a. Saline-epinephrine solution injection into subserosa to separate serosa from muscular layer
    - b. Tube identified on transection; proximal portion ligated and buried beneath the serosa
    - c. Low failure rate
    - d. Easily reversible
  5. Cook technique
    - a. Tube incised

- b. Proximal end ligated and buried in round ligament
- c. Distal end ligated and not buried
- d. Failure rate: 1-4/1000

C. Mini laparotomy

- 1. Done electively, usually postpartum
- 2. Techniques available: Pomeroy, Uchida, Cook
- 3. Contraindications
  - a. Morbid obesity
  - b. Fixed, retroverted uterus (unless postpartum)
  - c. Massive adhesions
- 4. Timing of postpartum procedures is important
  - a. Immediately after delivery--at delivery is technically possible, but does not allow much time to assess infant
  - b. 12-24 hours after delivery: may be associated with less postpartum hemorrhage
  - c. Up to 3-5 days postpartum: more technically challenging but feasible
  - d. >7 days after delivery
    - (1) Risk of infection is high
    - (2) Recommendation is to wait until uterus is fully involuted (30 days)
  - e. Small studies found that breast feeding women have decreased milk production if the procedure is delayed until 4-7 days postpartum

D. Laparoscopy revolutionized female sterilization

- 1. Electrosurgery/electrocautery
  - a. Unipolar electrosurgery
    - (1) Current applied to the fallopian tube but must pass through the patient's body to the ground plate attached to the patient's leg or buttock. Rare but devastating complication is "bowel burn" (resulting from spark?) causing necrosis
    - (2) Rapid destruction of considerable amount tube
    - (3) Rarely reversible
  - b. Bipolar electrosurgery
    - (1) High frequency current is applied from one tong through tissue to other tong
    - (2) Better control of tissue damage, although still relatively large area of thermal damage
  - c. Electrocautery--Waters technique
    - (1) Heat is applied to tube through metal hook, which catches fallopian tube and draws it into insulated sheath
    - (2) Within sheath, tube is coagulated and separates spontaneously to return to anatomical position

- d. Thermocoagulation--low voltage method
  - (1) More popular in Europe
  - (2) The current produced heats element used to burn selected portion of tube
- 2. Occlusive methods
  - a. Falope ring
    - (1) Ring applied through a minilaparotomy or double puncture laparoscopic technique
    - (2) Small silastic ring loaded into cylinder, into which a loop of tube is introduced
    - (3) Ring is pushed downwards to rest at base of the knuckle of tube (similar to Madlener technique)
    - (4) Reportedly higher levels of dysmenorrhea and cramping pain
  - b. Hulka clip
    - (1) Plastic core covered by gold-plated stainless steel spring to keep it closed
    - (2) Interlocking grooves on inner surface keep clip in fixed position
  - c. Filshie clip
    - (1) Inner surface is lined with silicone
    - (2) Minimizes dead space
    - (3) Applies uniform pressure on tube

### III. Failure Rates

- A. Range of 1-10/1000 women over 10 year period
- B. Failure rates for tubal sterilization depend upon techniques used and pregnancy status of patient
- C. Most failures with banding or clip application occur early
- D. Those with coagulation techniques tend to occur after customary 1-2 year follow-up period

### IV. Short-term Complications

- A. CDC defined categories of intraoperative and postoperative complications to permit comparison between methods
- B. Death---very rare
  - 1. CDC surveillance study using 1979-1980 data from Commission of Professional and Hospital Activities found 4 deaths among 376,335 women for a case fatality rate of 1.5 per 100,000 procedures. Others quote 3-4/100,000
  - 2. Complications of general anesthesia are leading cause of sterilization- attributable deaths
- C. Major vessel laceration from trocar or needle insertion occurs in estimated 1-10/10,000 cases
- D. Thermal bowel injury occurs 1/1,000 cases. This was attributable to unipolar devices primarily

- E. Luteal phase pregnancies or pregnancies which occurred prior to sterilization account for up to 30% of all sterilization failures
  - 1. D&Cs done at the time of surgery are generally poorly timed and do not prevent these pregnancies effectively
  - 2. Appropriately timed surgery or effective contraception until surgery is recommended

## V. Long-term Complications

- A. "Post-tubal syndrome" (PTS) is imperfectly defined but generally includes irregular cycles, menometrorrhagia, dysmenorrhea
  - 1. Problems in establishing existence of PTS
    - a. Many women will develop menstrual disturbances as they age, with or without sterilization
    - b. Post-tubal problems may have been masked prior to procedure by other methods (eg, OCs)
    - c. Most studies followed women for only short periods of time
  - 2. More current, longer term studies have indicated that some types of sterilization may carry higher risk for PTS
    - a. Procedures which destroy more of the tube are associated with PTS, especially dysmenorrhea
    - b. It frequently takes up to 5--7 years for PTS to become apparent
    - c. Women with presterilization problems have higher risk of having exacerbation of those problems
- B. Increased hysterectomy rates
  - 1. No good information available now, pending results of CDC's Collaborate Review of Sterilization (CREST)
  - 2. Possible explanations if true
    - a. PTS exists and menstrual abnormalities require surgery
    - b. Tubal sterilization changes physician and patient threshold for intervening surgically
- C. Ectopic pregnancy risk
  - 1. Early reports suggested increased risk of ectopic pregnancy. More recent studies have found that the risk of ectopic pregnancy is greatly reduced relative to the noncontraceptive user because the total pregnancy rate is reduced
  - 2. Risk of extrauterine implantation is increased and may be as high as 15-20%
  - 3. Method-related risk--coagulation techniques have higher

rates (3x) than do mechanical occlusion techniques or Pomeroy sterilization procedure

4. Mechanism
  - a. Uteroperitoneal fistula after unipolar electrosurgery
  - b. Inadequate coagulation or recanalization after bipolar procedures
  - c. Recanalization or fistula formation after Pomeroy, clip, or ring procedure
- D. Regret and desire for reversibility
  1. 2-25 % of women regret sterilization
  2. CREST study found
    - a. 4% expressed regret after 5 years
    - b. 6 % request information about reanastomosis
  3. Risk factors: young age and low parity were independent predictors of regret
  4. Other factors from international studies
    - a. Abrupt decision for sterilization before and/or after delivery
    - b. Decision made by person other than patient (husband, doctor, etc.)

## VI. Reversibility

- A. Depends upon technique used, location of defect, and amount of residual functional tube
- B. Many women will not be candidates
- C. Success rates, assuming at least 7 cm of tube:
  1. Unipolar: 41%
  2. Pomeroy: 50%
  3. Falope ring: 25 %
  4. Hulka clip: 85%

## Natural Family Planning and Fertility Awareness

- I. Definitions
  - A. Natural family planning uses a number of techniques to detect when a woman may be fertile and advocates abstinence during that time
  - B. Fertility awareness uses those same techniques to detect fertility but the couple uses some method of contraception (usually barrier or chemical methods) during the fertile period
- II. General
  - A. Failure rate varies with techniques used, predictability of woman's cycle and compliance of couple
    1. Perfect use failure rate for postovulatory intercourse only is 11%

2. Typical use failure rate is 20%
- B. Much of technology used with these methods developed to assist infertile couples achieve pregnancy
- C. Continuation rates after 1 year
  1. 84% (excluding pregnancy)
  2. 67% (including pregnancy)

### III. Several Techniques Available to Guide Patients in Periodic Abstinence

- A. Calendar "rhythm" rarely used today by itself
- B. Temperature (thermal)
- C. Cervical mucus method
- D. Sympto-thermal method (STM)

### IV. Menstrual charting (calendar or rhythm)

- A. Failure rate for perfect use is 9 % . Lowest reported rate is 14.4%
- B. Sperm viability in the female reproductive tract is 27 days and the life span of the ovum is 72 hours. Therefore, span of fertility may be from 7 days before ovulation to 3 days after. However, most systems shorten those estimates to increase compliance. In most calendars used, the assumptions are:
  1. Ovulation occurs 14 days before onset of next menses of cycle ( $\pm 2$  days)
  2. Sperm remain viable for 2-3 days
  3. Ovum survives 24 hours
- C. Patient keeps menstrual calendar for 8 months, then applies the following formulas to the collected data
  1. Earliest day of fertile period = number of days of shortest cycle length minus 18 days
  2. Latest day of fertile period = number of days of longest cycle length minus 11 days
- D. Tables are useful

# Days of <u>Shortest Cycle</u>	First <u>Unsafe Day</u>	Days of <u>Longest Cycle</u>	Last <u>Unsafe</u> <u>Day</u>
21	3	21	10
22	4	22	11
23	5	23	12
24	6	24	13
25	7	25	14
26	8	26	15
27	9	27	16
28	10	28	17
29	11	29	18

30	12	30	19
31	13	31	20
32	14	32	21
33	15	33	22
34	16	34	23
35	17	35	24

- E. Example: a woman with cycles varying from 25-31 days has a calculated fertility period each month between days 7 and 20
- F. New devices being marketed to assist patients in remembering fertile days---eg, Swiss Lady Watch is wrist watch which patient resets each month at the first day of her cycle to tell her which dates are relatively safe
- G. Problems with method
  1. Prolonged periods of abstinence required
  2. Not applicable to women with irregular menses
  3. Breast-feeding women may have no menses to chart.
  4. Question of what method to use during data-gathering months

**V. Basal body temperature (thermal) method**

- A. Failure rates for postovulatory methods in perfect users are theoretically as low as 1-2%. Lowest reported failure rate is 10.5%
- B. Technique based on observation that some women will experience drop in BBT just prior to ovulation and many women will experience increase in temperature 24-72 hours after estrogen peak (approximate time of ovulation)
- C. Method used to determine when ovulation has occurred and infertile period has begun. Couple may engage in intercourse only after patient has had a sustained temperature rise for at least 3 consecutive days
- D. Problems
  1. No advance warning of impending ovulation. Therefore, preovulatory intercourse after day 4 of cycle may be forbidden
  2. Up to 20 % of women may have no interpretable biphasic BBT pattern
  3. Disruption in biphasic pattern can be caused by illness, jet lag, stress, sleep interruptions
  4. Difficult to teach and to interpret BBT method

## VI. Cervical Mucus Method

- A. Failure rate for perfect use is 3%. Life table analysis of 12 month typical failure rates is 16-25%; lowest reported failure rate is 10.5%
- B. Cervical mucus changes in response to estrogen levels
  1. Postmenstrual infertile days: cervical mucus undetectable or scant
  2. Fertile days: cervical mucus changes as protein, polypeptide, and sodium content changes
    - a. Preovulation: mucus cloudy, yellow or white, sticky
    - b. Ovulation: mucus wet, slippery, clear
    - c. Postovulation: mucus thick, cloudy, sticky
  3. Postovulatory infertile days cervical mucus undetectable or scant
- C. Techniques
  1. Prior to urination, patient checks the mucus on her vulva or introitus with her fingers or a piece of tissue. The sample is analyzed for its general appearance, its slipperiness and elasticity
  2. During fertile period, total abstinence is practiced until the 4th day after peak mucus production
  3. During preovulatory period, abstinence is necessary on the day after each act of intercourse so that mucus changes will not be misinterpreted
- D. Training
  1. It may take several months for a patient to learn her normal cycle
  2. Partners must abstain from intercourse during this time so as not to cloud the patient's findings
  3. Use of condoms is not adequate, since sexual arousal will increase vaginal secretions and confuse the results

## VII. Symptothermal Method (STM)

- A. Failure rate for perfect use is 2%. Life table analysis of 12 month failure rate is 11-20%. Lowest reported failure rate (pearl index) is 12.6%
- B. Utilizes a wide variety of techniques to detect fertile period
  1. Usually combines cervical mucus changes with measurement of basal body temperature
  2. Recognizes other signs
    - a. Mittelschmerz
    - b. Cervical changes (texture, position, and dilatation)
    - c. Change in libido
- C. Other techniques may be added as technology improves

In 1982, the IUD made up about 7% of the contraceptive market. In 1987, it made up 3% of the contraceptive market. The main reason for the Dalkon shield's increased risk of pelvic inflammatory disease in tubal ovarian abscess was its multi-filament wrapped tail that was coated with plastic.

In China, IUDs make up about 25% of the contraceptive market. IUDs are meant as a permanent form of contraception and therefore IUDs are inserted into the uterus without a string because they are not thinking about going back in and taking them out. The data from China shows that an IUD without a string doesn't cause pelvic inflammatory disease. Then bacteria could get inside the plastic, crawl its way up through the interstices of the wrapped multi-filament tail, jump out here, get into the uterus, get into the tubes. In fact, there are some nice electron micrographic photos of bacteria doing just that. Kind of weaving their way up through the string and popping out and leading to this 8-fold increase in the relative risk of pelvic inflammatory disease associated with the Dalkon shield.

Now that we have a new copper IUD out on the market to go along with Progestasert, we have two forms of IUDs that we can use. The Progestasert, as you know, is only active for one year. The new ParaGard is active for 10 years. The compelling reason to use a longer lasting IUD is that the greatest risk of pelvic inflammatory disease is in the first two months after insertion. Therefore, after that the risk goes back down to the baseline level which means that the greatest risk is if you put an IUD through a cervix that is infected with bad pathogens. Everybody who gets an IUD inserted has bacteria in their uterus for the first 48 hours after an IUD is inserted. So if you have bad pathogens, they are going into the uterus, they could set up PID and so you need to screen your patients to make sure that they are not at a risk for having bad pathogens colonizing their cervix that will get dragged up into the endometrium.

How do IUDs work? They interfere with sperm transport, they interfere with the fertilization, they interfere with implantation. Because people are under the general impression that IUDs act primarily as an abortifacient when they act more specifically to make sure that the sperm and the egg do not get together to lead to fertilization. The IUD decreases sperm transport, it is spermicidal and you see very few fertilized oocytes in patients that have IUDs. You see very few cycles that are associated with an hCG rise and so the main effect is inhibiting fertilization.

The first 12 months of IUD use, is associated with an 0.7% risk of pregnancy. That risk after four years is 1.3%. The main reason for removing the IUD, is pain and bleeding. After four years, the cumulative rate is about 38%.

Why do patients get pregnant with an IUD? A study in the *Green Journal*. Found that about 52% of pregnant women with an IUD, the IUD was located away from the fundus of the uterus. So if you see a patient whose string keeps growing, strings don't grow. That means that the IUD is slipping down. Its efficacy is decreased and you need to remove it. The other part of that slide was that it doesn't matter when you insert the IUD in the menstrual cycle. That does not matter in whether the IUD slides down into a lower position in the uterus. But if the string starts growing, that IUD should be taken out.

What happens when a patient becomes pregnant? About 50% of the time, if the IUD is left in place, they will have a spontaneous abortion. If the IUD is expelled or removed, that goes back down to the normal background normal spontaneous abortion rate. If you pull the IUD with the pregnancy, it does not precipitate a spontaneous abortion. Studies have looked at the spontaneous abortion rate within the first month after an IUD has been removed because of a pregnancy and it doesn't increase the risk of spontaneous abortion. We do know if the IUD is left in place that the risk of preterm labor is increased. If a patient does become pregnant and has a spontaneous abortion, there is a greater chance that she will become a septic spontaneous abortion.

What is the chance of a woman having fertility problems after stopping various forms of contraception? As you can see for the IUD, oral contraceptive, diaphragm and other methods, after three to four years, there is no difference in fecundity and fertility. This is the normal background of infertility in the United States. The first year after discontinuing oral contraceptives, you see a number of women that have become pregnant because a lot of these were anovulatory before they were started on oral contraceptives. They were started on oral contraceptives for their period regulating effect meaning that they were anovulatory and therefore they will be anovulatory for the first six to 12 months after discontinuing oral contraceptives.

What is the chance of a patient developing an ectopic pregnancy if they become pregnant? Well, the bottom line is usually where you will find the most important information. The risk of ectopic implantation if the woman becomes pregnant with the IUD is 5%. That is for the copper IUDs. The progesterone IUDs is slightly

## VIII. Overall Limitations of Natural Family Planning Methods

- A. Requires patience, motivation, cooperation, and self-control from both partners
- B. Requires considerable patient education
- C. May not be suitable for women with irregular menses or breast feeding
- D. Note: careful clinical studies have not found an increase in spontaneous abortion rates or risk of congenital abnormalities as some were expecting from "old egg" or sperm failures

## IX. Benefits of Method

- A. Acceptable to religious groups opposed to other methods of contraception
- B. Teaches couples much about reproduction and their own bodies

## Intrauterine Contraceptive Devices (IUDs)

### I. History

- A. Development of the IUD
  - 1. 1909 Richter used a circle of string made from silkworm gut as an intrauterine contraceptive device
  - 2. 1930s--Grafenberg added a wire ring of copper, nickel, and/or zinc to hold the gut in place
  - 3. 1934----Ota developed a ring of gold or gold-plated silver
- B. Modern IUDs
  - 1. In the 1960s, nonmedicated, biosafe plastic IUDs were introduced
  - 2. In the 1970s, the medicated RID containing copper (copper T-shaped device) was developed. An RID with a progesterone reservoir (Progestasert) was also developed during this time period
- C. Disappearance of the IUD
  - 1. In 1982, IUDs made up 7% of all contraceptive methods used. This decreased to 3% by 1987
  - 2. One particular plastic IUD (the Dalkon Shield) with a multifilamentous string was associated with a high incidence of pelvic infections, which precipitated a large number of personal injury litigation cases
  - 3. Other IUD manufacturers voluntarily removed IUDs from the market. FDA has never withdrawn approval for IUD use
  - 4. Progesterone-secreting IUD (Progestasert) retained position in market. Pioneered patient consent forms
- D. Newest IUD Copper T-380A-ParaGard

higher. The same thing with Norplant. Twenty seven percent of pregnancies with Norplant will be ectopic. The same thing with Depo. About 10% of pregnancies associated with Depo will be ectopic. That is possibly because of the decrease in tubal motility associated with a progesterone containing contraceptive method that leads to this increased risk. But if you look at a less than 1% risk of pregnancy and 5% of those implanting ectopically, the total number of ectopic pregnancies associated with this form of contraception is still less than not using any form of contraception.

The main reason why people do not use IUDs is because of the risk of pelvic inflammatory disease. This is the study I alluded to before. This was a fairly recent study from Dan Michell in 1966 where they looked at endometrial cultures done transfundally, which is why you probably can't get a lot of patients to agree to this study today. I don't know how he got those at USC back in those days, but 100% had positive cultures in the first day and that dropped fairly rapidly down to a low percentage. You do not want to put an IUD in a patient that has significant pathogens of their cervix. Again, the greatest risk of pelvic inflammatory disease is within the first one to two months after insertion. After two months, the risk of pelvic inflammatory disease is not statistically elevated. Again, if you put an IUD in a patient that had cervical pathogens that could lead to an upper tract disease, they are going to get an upper tract disease.

IUDs are the only true patient risk factor associated with bacterial vaginosis. IUDs increase the number of anaerobes in the vaginal flora, increase the risk of bacterial vaginosis. They do not change the risk of Candidiasis and trichomoniasis. IUDs and Actinomyces, this is an opportunistic infestation, not a true infection. Remove the IUD and repeat the pap smear after the next menses. Patients do not need any penicillin containing antibiotic regimen to hasten the removal or disappearance of the Actinomyces from their lower genital tract. If they do develop a PID or a tubal ovarian abscess associated with Actinomyces, they do need penicillin. If after one or two cycles, the patient hasn't cleared their Actinomyces, then give them some kind of antibiotic regimen.

Abnormal cytology. To treat abnormal cytology, you should remove the IUD because if you laser or freezing of the cervix, that might increase the uterine contractility and therefore push the IUD down away from the fundus. IUDs do not increase the risk of abnormal cytology or increase the risk of endometrial cancer.

Perforation rates are very low. They are less than 1 in 1,000.

Menstrual blood loss is also increased except for the progesterone containing IUD. That is probably the main reason to use these IUDs where the patient wants an IUD but can't tolerate the bleeding associated with it. Studies have shown that if you give a patient a nonsteroidal anti-inflammatory you can decrease the bleeding associated with the IUD.

Norplant has been studied extensively by the Population Council. There are currently probably twice this number of women that are using it or have used it in the United States. You know that they are six soft Silastic capsules. This is their diameter. They have levonorgestrel. The levonorgestrel slowly leeches out over five years. There is a levonorgestrel containing IUD in Europe.

The main problem with Norplant is that these capsules are not biodegradable. It's long lasting.

It suppresses ovulation. However, in the first couple of years, you see very few ovulatory cycles but after about three years, 60% of cycles are ovulatory. Just like OCs and Depo, the nonovulatory inhibiting effect is just as important as the ovulatory inhibiting effect in decreasing pregnancy. Cervical mucus gets thickened. The endometrium gets atrophic and those are the equally important mechanisms of action for these forms of contraception that contain progesterone.

There was this data that suggested that the bigger the patient weightwise, not sizewise, the greater the risk of failure. This data has been reworked and the numbers really aren't as high as this. There is some suggestion that weight does play a role, in failure but it is not to the cumulative pregnancy rate of 8% that was suggested in some of the earlier work.

Some of the risks. The absolute risk of ectopic pregnancy is over 20%. The absolute number of ectopic pregnancies are decreased because the pregnancy rate is less than 1%. If a patient does become pregnant because of the levonorgestrel, since it is a fairly androgenic progestogen, there is a risk of masculinizing a female fetus. But there is no data in the literature that this has ever happened in women that become pregnant.

What are the menstrual cycle changes? About one-third of women will have amenorrhea, about a third of women will have subtle changes in the length and

1. T shape conforms to a maximally contracted uterus so it has less impact on the endometrium
2. Monofilament string of polyethylene is less likely to allow bacteria to ascend into uterus

## II. Mechanism of Action

- A. IUD decreases the number and penetrability of sperm
- B. Inhibits sperm mobility through the uterus
- C. Inhibits fertilization
- D. Impairs ovum transport through fallopian tube
- E. Foreign body leads to low grade inflammatory response, which may decrease nidation

## III. Risk of Unwanted Pregnancy

- A. First year failure rate: 0.7--0.8% (Pearl index)---ParaGard

$$\text{Pearl index} = \frac{\text{Number of pregnancies}}{\text{Number of women-years}} \times 100$$

- B. Cumulative net pregnancy rate after 4 years: 1-3 per 100 women
- C. The highest pregnancy rates are within the first year after insertion and are highest for younger women

## IV. Event Rates

- A. Expulsion rates after 4 years are 9.2 per 100 women. The rates are highest in the first year and are lowest for the oldest patients
- B. Perforation rates are 0.5%, with 80% being transcervical
- C. Removal for pain and bleeding is 11% per year (36% after 4 years). This rate is lowest in women over 25 years of age
- D. Removal for medical reasons
  1. Pelvic inflammatory diseases 2.5%
  2. Endometritis 0.2%
  3. Vaginitis and vaginal discharge 11%
- E. Cumulative continuation rate after 4 years is 31.8 per 100 women and is higher as the patient becomes older

## V. Fertility After Stopping IUD

- A. The percentage of patients desiring pregnancy and remaining undelivered after 42 months of stopping a contraceptive agent was 6.0% for the IUD, 4.0% for oral contraceptives, and 4.0% for the diaphragm
- B. There is no prolonged impairment of fertility in women who stop using the IUD for a planned pregnancy

## VI. Outcome of Accidental Pregnancies

- A. If the IUD is left in place with the strings protruding through the cervix, there is a 54% incidence of spontaneous abortion

flow of their period, about a third of women will have spotting and bleeding and these are the women that really dislike their Norplant. This resolves in the majority of cases in about three to six months. At the end of four years, 10-20% of women might still be experiencing it.

How do you manage the menstrual changes? You can try nonsteroidals. You can give the patient ethinyl estradiol. Or you can remove the capsules. There is some effective Norplant on glucose tolerance. There is a slight change in the lipid profile. Not to the same extent as oral contraceptives because the serum levels of the levonorgestrel are very, very low. Coagulation factors are not significantly changed. About 50% of women will gain weight and about a third of women will lose weight but they will not gain weight to the same degree that they do on Depo-Provera however.

We know that Depo-Provera is a very effective form of contraception. It has a very high continuation rate.

Just like Norplant, Depo-Provera is associated with menstrual changes and it is related to use. As you can see out here, after a year, amenorrhea in about 45%. Infrequent menses, about 37%. Frequent menses, about 5%. Irregular or prolonged menses together make up about 20% and, again, these are the patients that are very unhappy with that form of contraception.

Weight gain is a significant problem and women on Depo-Provera can gain a significant amount of weight. If they can't tolerate weight gain, this is not the form of contraception for them. The same mechanism of action because it is a progesterone form of contraception. So you inhibit ovulation, thin out the endometrium, thicken the cervical mucus and you change tubal motility so you have an increased risk of ectopic pregnancy.

The other main problem with Depo-Provera is that it takes a long time to get pregnant after the last injection. It also can take a long time for the patient's menstrual pattern to regulate. Warn patients of that. The time for conception is anywhere from 4-24 months, a mean of about 10-12 months. It is not related to the number of injections or how long they have been on the Depo. It does seem to be related to how big they are. The higher their body mass or the higher the number of adipose cells, the greater the chance of them having a fairly long time to be able to conceive.

Natural family planning methods are a very important consideration for a fairly small subset of patients. Particularly ones that are in a stable relationship. Find out when a patient's fertile period is and have them avoid having intercourse during that fertile period.

Failure rates are fairly high and they vary with the technique. If you have perfect use with inhibiting postovulation intercourse, the pregnancy rate should be about 1%. Typical failure rate is around 20%. It does have a high continuation rate because these tend to be very motivated patients and they are using this for various personal reasons which fit into their lifestyle.

The calendar method, the temperature method, the cervical mucus method and then the symptom and temperature method. Therefore the patient really is just abstaining from having sexual intercourse because there is no time that they can have intercourse using that method.

The menstrual charting method has a perfect failure rate of 9%. The lowest reported failure rate is about 15%. Remember sperm is viable for two to three days but there are some super sperm out there that can live for about seven. The ovum usually survives for about 24-48 hours. Really, the ova tend not to last as long as the supersperm do. 48 hours after ovulation, the chance of getting pregnant is very low. But the chance of getting pregnant is much higher if they have intercourse before ovulation, even up to seven days before ovulation. The period from menses to ovulation is less consistent than the time frame from ovulation to the next menses which is 14 days.

Breast feeding women don't usually have any menses. There are a number of women that can get pregnant while they are breast feeding. It is a good form of contraception, but it is not absolute.

We know that basal body temperature can be used as a method of predicting ovulation. Basal body temperature drops prior to ovulation. Then we see a temperature peak, 24-72 hours after the estrogen peak. Then three days after the initial drop and then rise, patients can start having intercourse because they have ovulated and the egg is dead. The problem is, having intercourse before the fertile period. Look to see how vigorous the sperm are because sperm viability is the greatest variable in the survival of the sperm and the egg.

(based on older Dalkon Shield data). The risk of septic abortion is 2%, which does not exceed the baseline rate of abortions developing septic complications. (The risk of septic abortions was higher for the Dalkon Shield)

- B. The risk of spontaneous abortion decreases to 20% if the IUD is removed
- C. The risk of preterm labor is increased if the IUD is left in place (17.4%) rather than removed (4.3%)
- D. The risk of stillbirth, congenital abnormalities, or other pregnancy complications is not increased if the IUD is left in place
- E. Management of IUD if pregnancy occurs
  - 1. If string is visible in the first trimester, removal is indicated. If the patient has more advanced gestational age, the likelihood of seeing the string is lower and an ultrasound prior to removal may be warranted to evaluate the relationship of the IUD and placenta
  - 2. If string is not visible, confirm with ultrasound that the IUD is still in utero and counsel the patient appropriately. Patient with IUD in utero needs to know it will not increase risk of birth defect, but should be alert to signs of infection

## VII. Management of Missing String in the Nonpregnant Patient

- A. Document that patient is not pregnant
- B. Gently probe cervical canal and lower uterine segment (endocervical speculum may be helpful)
- C. Ultrasound or x-ray to distinguish between perforation, silent expulsion, or retained IUD with string raised
- D. Remove IUD with Rocket forceps if possible
- E. Hysteroscopy for removal if imbedded into myometrium
- F. Role of laparoscopy questioned with copper IUD perforation

## VIII. Risk of Ectopic Pregnancy

- A. Relative risk of ectopic pregnancy reduced (0.4) with IUD use
- B. IUD protects better against intrauterine pregnancy than against extrauterine implantation
  - 1. If a woman becomes pregnant with the ParaGard, there is a 5% chance that this will be ectopic
  - 2. The risk may be greater for the progesterone IUDs

## IX. PID

- A. Older, uncontrolled studies demonstrated the relative risk of developing PID for various IUDs
  - 1. Nonmedicated and copper IUDs: 1.2
  - 2. Progesterone IUDs: 2.2
  - 3. Dalkon Shield: 8.3
- B. The risk of PID is highest for the first 3 months after insertion
- C. Re-analysis of PID risk using traditional STD risk factors shows:

Problems with basal body temperature charting. There is no warning for impending ovulation. Combine this with the menstrual charting technique so that the patient knows when to start anticipating ovulation. It is easier to figure out when they can resume having intercourse than when they should stop having intercourse with this method. Jet lag messes up basal body temperature charting and a number of women have uninterpretable basal body temperature charts. So stewardesses can't use it. Patients that have uninterpretable basal body temperature charts can't use it.

Cervical mucus has a fairly high failure rate. The cervical mucus changes in response to estrogen. Estrogen is a predictor of impending ovulation so you go from a thick, cloudy mucus to a clear watery mucus. Then after the fertile period is over, the mucus gets undetectable and scant.

Check their cervical mucus prior to urination. Look at the introitus or inside the vulva, analyze it for its slippery, elastic contour. They can resume having intercourse four days after the peak wateriness of the cervical mucus.

Barrier methods. Twenty-two percent of oral contraceptive users are using condoms. Seven percent of sterilized women are using condoms and 50% of condoms are being purchased in the United States by women. A number of women are beginning to realize that condoms can prevent sexually transmitted diseases and are a good method of contraception.

We used to see a lot of condom use in married women. But the number of unmarried women that are using condoms is also on the rise so there is a lot of condom use out there. Condoms can break and condoms can fall off. Condoms break in about 1 out of every 162 acts of intercourse. The risk of breakage is greater without lubrication. The failure rate for condoms, if you look at a patient who is using spermicide, it is about 10%. If you look at women over the age of 30 who are using spermicide, the failure rate is only about 4%. Just like diaphragms, all barrier methods tend to be a better form of contraception in someone whose fecundity is starting to drop or who are having intercourse less frequently than three times a week.

The reality condom, the failure rate is quoted anywhere from 12-25%. The reason why the reality condom got through the FDA so quickly is it was felt that there was a need for some method of STD and pregnancy protection that the female could use irrespective of what her partner's choices were. It will help against vaginal vulvar STDs. It is a polyurethane cover. Add spermicide. Just remember that if you use a female condom, don't use the male condom at the same time because the latex will rub against the polyurethane and will disintegrate the reality condom.

Diaphragms are a very good form of contraception. The failure rate is anywhere from 2-20% closer to about 15-18%. Again, it is a more effective method for more mature women, who are having less frequent episodes of intercourse per week. It needs to be properly fitted. It covers the sperm to prevent entry. It also localizes the spermicide so that it has the greatest action and that improves its contraceptive efficacy. There is some suggestion that diaphragms increase the transmission risk for HIV because of the microabrasions that are created in the cervix from the diaphragm. However, this has not been supported by the literature. Fit it between the cervix and the posterior area of the symphysis pubis. If it is too tight, it will obstruct the urethra. If it is too loose, it can get dislodged during intercourse and therefore decrease its contraceptive effect.

It needs to be changed or refitted every two years, if there is a 20% change in weight or if the patient has had a term delivery or a second trimester pregnancy loss. It must be used with a spermicide. It needs to be in place at least half an hour, preferably longer, before intercourse. It needs to stay in for six hours after the last act of intercourse. For each act of intercourse, more spermicide needs to be added.

Remember that the nonoxynol-9 is a very good form of medication to use because of its virucidal and bactericidal effect. nonoxynol-9 is one of the few things that will kill the human papilloma virus.

Cervical caps. Their failure rate is comparable to the diaphragm. It protects the cervix from sperm entry because it is covering the cervix and it localizes the spermicide. At least the Prentif cervical cap comes in four sizes. Most of the other cervical caps come in a limited number of sizes. Since most cervical caps need to be fitted, there will not be an over-the-counter cervical cap.

There are various numbers of vaginal spermicides. They all have a certain time frame between when you insert them and when they become active. Suppositories can take up to 30 minutes. Foaming tablets about 15 minutes. The aerosols are instantly active. Once the jellies hit body temperature they are active and creams must also hit body temperature.

1. No increased risk for PID in IUD users who are married or in otherwise monogamous relationship
2. No increased risk in tubal infertility in IUD users with one partner. Risk doubled over nonusers if multiple partners

Failure rate is fairly high. It acts as a detergent and a surfactant. It can prevent bacterial and viral STDs because they are bactericidal and virucidal and just like latex condoms, there are about 2-4% of patients that are allergic to it.

## X. Criteria of IUD Candidates

- A. Women who are in stable, mutually monogamous relationship
- B. Parous (proven fertility)
- C. Absence of anything in patient's history which indicates she has compromised her fertility
- D. Anything in her current situation which suggests she may be at risk for acquiring a STD
- E. Meets criteria listed in informed consent. Since introduction of detailed patient evaluation and informed consent process, there have been no lawsuits against IUD.

## Oral Contraceptives

### I. General

- A. OCs are the most completely studied drugs in history
- B. Many concerns were based on anecdotal data or on using pills with higher doses of hormones than current formulations have
- C. The trend in recent years has been to recognize that the contraceptive benefits clearly outweigh the risks and that noncontraceptive benefits are an important element in the equation
- D. Significant gap still exists between what physicians know and what patients believe

### II. Failure Rates

- A. Pearl index (# pregnancies/100 woman years of use)
- B. Theoretical failure rate or method failure rate first year 0.3 %
- C. Typical use failure rate 2.5-3%, although in first year, rates up to 8% are not uncommon

### III. Contraindications

- A. Absolute contraindications have been significantly reduced over time as hormone levels in pills have plummeted
- B. Today's low dose pills are absolutely contraindicated only in the following cases:
  1. Thrombophlebitis or thromboembolic disorders or history thereof
  2. Cardiovascular or coronary artery disease
  3. Known or suspected carcinoma of the breast
  4. Carcinoma of the endometrium or other known or suspected estrogen- dependent neoplasia

5. Undiagnosed abnormal genital bleeding
6. Cholestatic jaundice of pregnancy or jaundice with prior pill use
7. Hepatic adenomas or carcinomas
8. Known or suspected pregnancy
9. Current use of rifampin
10. Strongly contraindicated in older women who smoke
11. Malabsorption syndromes (active disease)

#### IV. Cardiovascular Impacts

- A. Origin of concerns
  1. Early work in 1960s and 1970s suggested that women who had heart attacks were more likely to have taken OCs
  2. Reanalysis considering other risk factors, such as hypertension and previous CAD, demonstrates that OC use, by itself, was not increased in a woman who had premature cardiovascular accident
- B. Impact of traditional pills on lipid profile is minimally adverse
  1. Atherosclerosis is a progressive disease which starts very early in Americans
  2. The Framingham study of men aged 55-65 and clinical studies working with subjects who have hyperlipidemia demonstrate that for every 1% increase in cholesterol, there is 2% increase in risk of coronary artery disease
  3. Older formulations of OCs caused cholesterol and LDL subfractions to increase about 1%
  4. Appropriateness of extrapolating Framingham findings to women of reproductive age using the pill has been called into question
- C. Impact of pill on CVD
  1. Heart attacks and cerebrovascular accidents in pill users are thrombotic problems, not atherosclerotic ones
    - a. Ex-users of pills have no increased risks over new users
    - b. Duration of use does not increase risk for CV disease
  2. Animal data demonstrate disassociation between serum lipid profiles and atherosclerosis in pill use
  3. Clinical studies uniformly demonstrate no increase risk of CV disease with low dose OC use in women
    - a. There are no prospective, double blind, randomized clinical trials to establish OC safety
    - b. No MIs or CVA in OC users
    - c. Relative risk for MI in OC users = 0.9
    - d. Current OC users had no increased risks for acute MI, ischemic heart disease, pulmonary embolism, or

thrombophlebitis

- e. Among nonsmokers, there was no increase in incidence of MI in OC users
  - f. Past use of older high-dose OCs did not increase risk of subsequently developing cardiovascular disease at least up to age 60
- D. New progestins (Norgestimate and Desogen) are less androgenic and are lipid-neutral. May be best choice for women with increased risk for CVD
- E. Clinical significance: women may use OCs past age 40
- 1. 1990 FDA labeling change

"The suggestion that women over 40 who don't smoke should not take oral contraceptives is based on information from older, high-dose pills and on less-selective use of pills than is practiced today. An advisory committee of the FDA discussed this issue in 1987 and recommended that the benefits of oral contraceptive use by healthy, non-smoking women over 40 years of age may outweigh the possible risks. However, all women, especially older women are cautioned to use the lowest-dose pill that is effective"

- 2. ACOG guidelines for OC use in women over 40 (very strict)
  - a. Nonsmokers
  - b. <30% above ideal body weight
  - c. Normal glucose screening test
  - d. No family history of CVD before age 50
  - e. Negative mammography
  - f. Normal lipid profile
  - g. No other contraindications
- 3. Detection of menopause in women on OCs. Switching to HRT:
  - a. If a woman continues to use a low dose OC until menopause, symptoms of estrogen deficiency may not be apparent. However, serum FSH levels drawn on days 5-7 of placebo pills will rise normally in a perimenopausal woman on OCs
  - b. Switch from OCs to HRT. Dose of OC is 8-20 times higher than needed for physiologic replacement

## V. OC and Cancer

- A. Protective effects of OCs
- 1. Ovarian cancer
    - a. Risk reduced in nearly 40% of "ever users"
    - b. Protection increases to over 80% with prolonged OC

- use (>10 years)
    - c. Protective effect lasts for at least 15 years after last use of pill
  - 2. Endometrial cancer
    - a. Risk reduced approximately 50% in "ever users"
    - b. Protection increases with longer use, although even short-term use offers some protection
    - c. Protective effect lasts for 15 years beyond time of last OC use
    - d. With even 12 months of use, 3 major types of endometrial cancer reduced
- 1. No increase in overall risk of breast cancer
- 2. OC users may have relative risk of 1.1 for developing premenopausal breast cancer
- 3. Postmenopausal breast cancer rates decreased
- 4. No group identified to be at higher risk (family history, benign breast disease, prolonged use of OCs, use of any formulation of OC). OC users have decrease in benign breast disease

## VI. Metabolic Effects by Hormone

- A. Both ethinyl estradiol and the progestins produce metabolic changes that may be implicated in clinical complications or side effects.
- B. Serious adverse effects

Cholelithiasis	2x	1:1,250
MI (smokers > 35)	3x	1:5,000
Thrombophlebitis	3x	1:10,000
Thromboembolism	4x	1:30,000
Stroke	3x	1:30,000
Liver Adenoma	500x	1:50,000
Mild Hypertension	2-3x	< 1:20

Figure 1: Metabolic Effects of Ethinyl Estradiol

Adipose cells	Hypertrophy Weight gain, increased fat
Serum lipids	deposits in hips, breasts, thighs Increased HDL-C Decreased risk for CAD Decreased LDL-C
Blood vessels cell activity	Decreased coronary artery foam Decreased atherosclerotic Cerebral vasospasm

	plaque. Headaches
Electrolytes	Sodium retention Edema, weight gain, headaches
CNS	Decreased serotonin Depression Increased prolactin Nausea, galactorrhea
Vitamins	Decreased B complex and C None Increased A None
Breast	Increased blood flow Breast swelling and tenderness
Skin	Stimulation of melanocytes Chloasma Decreased sebum Decreased aerie

## VII. New Progestins

- A. 3 new progestins-norgestimate, desogestrel, and gestodene- have been developed to increase the progesterone-receptor affinity and decrease androgenicity. The first 2 have been FDA-approved
- B. Prehormones designed to minimize androgenicity
  1. Androgenicity not needed for contraception
  2. Androgens have adverse impacts:
    - a. Lowers HDL, raises LDL
    - b. Weight gain, ache, hirsutism
    - c. May decrease patient compliance
- C. Relative affinity of these compounds for progesterone receptors versus androgen receptors greatly enhanced. Longer half-life
- D. Clinical trials substantiate bench findings
  1. SHBG levels increase over time; free testosterone levels drop
  2. LDL unchanged; HDL and triglycerides increase
  3. Minimal weight gain. Maximum average weight gain < 0.5 pounds
  4. Acne and hirsutism decreased
- E. Experts question significance of lipid neutrality in face of proven safety of low dose conventional pills. Recommendations:
  1. No need to switch patients who are successfully contracepting with older low dose formulations
  2. Consider newer formulations for higher risk patients and

perhaps teens

### VIII. Use of OC Pills in Women With Medical Problems

- A. Many of the past absolute contraindications to OC use have been reclassified as relative contraindications or completely resolved
1. Asymptomatic mitral valve prolapse without mitral atrial fibrillation
  2. Epilepsy: estrogen increases spike frequency and lowers seizure threshold. Progestin has opposite effects. On balance, OC causes no increase in seizure activity. Estrogen in OC will induce more rapid clearance of anticonvulsant medication. Therefore, therapeutic levels must be monitored. Higher doses of EE also needed
  3. Diabetes without vascular complications
  4. Hypertension
  5. Anticoagulated patients with valvular replacement
  6. Endocrinopathies: thyroids, prolactinomas, PCO
  7. Asthma-drug interaction potential exists here. Also estrogen can cause thickening of bronchial mucus to increase frequency or severity of attacks. However, most women tolerate well
  8. Previous gestational diabetes serial screening is necessary to detect progression of disease
  9. Sickle cell disease and wait----thrombosis affected by OCs uses different pathway than sickling phenomena. OC use not contraindicated and may sustain HBG
  10. Immune thrombocytopenic purpura
  11. Leiomyomata---no increased growth induced by OCs (progestin decreases estrogen receptors)
  12. Bleeding dyscrasia patients may benefit from ovulation suppression
  13. Previous preeclampsia. No increased risk of hypertension in OC users despite angiotensin sensitivity

**Figure 3 OC Use Questions OC Use Contraindicated**

<u>Clinical Problem</u>	<u>Yes</u>	<u>Absolute</u>	<u>Relative</u>
Hypertension--Uncontrolled		X	
Hypertension--Controlled	X		
Hypertension-Gestational	X		
Diabetes Mellitus---Vasc.		X	
Disease Diabetes Mellitus---No	X		
Vasc. Dis	X		
Diabetes Mellitus-Gestational			
Liver Die---Active		X	

Liver Disease-Past History	X		
Seizure Disorders	X		
Deep Venous Thrombosis		X	
Pulmonary Embolism		X	
Sickle Cell Disease	X		
Sickle Cell Trait	X		
Migraine Headache			
	X		
Organic Heart Disease		X	
Cerebrovascular Disease			X
Mitral Valve Prolapse (I)	X		
Mitral Valve Prolapse (II)			X
Prosthetic Heart Valve and Anticoagulation	X		
Breast Cancer		X	
Pituitary Prolactinoma			X
Leiomyomata Uteri	X		
> 35 Years, Healthy, Nonsmoker			X
> 35 Years, Smoker	X		
Teenager			
Severe Depression			X
Intestinal Malabsorption Disease		X	
Current Use of Rifampin		X	
Pregnancy		X	
Breast-feeding			X

B. Some medical conditions mandate close monitoring and a careful risk-benefit analysis prior to considering OC use

1. Systemic lupus erythematosus

- a. Case reports of increased flaring of lupus may make the combination OC undesirable choice, particularly with renal compromise
- b. The progestin-only pill may still be a good option for the normotensive patient with no renal compromise

2. Functional/structural heart disease

- a. Patients who are fully anticoagulated may greatly benefit from ovulation suppression and fertility control
- b. Careful evaluation of the impacts of fluid retention and possible adverse lipid profiles needed

3. Stable mild hypertension is clearly a gray area

- a. Women with few contraceptive options, normal lipid profiles, and normal renal function can be considered for combination OC

- b. Patients with labile or poorly controlled hypertension are not OC candidates
- 4. Malabsorption syndromes, such as Crohn's disease or ulcerative colitis, must be in remission before oral medication can be considered
- 5. Women on long-term antibiotic therapy must be permitted to reestablish bowel flora prior to OC use. Otherwise:
  - a. Enterohepatobiliary recirculation will not take place
  - b. Failure rates may increase
- 6. Renal transplant patients without underlying vascular disease may be candidates for OCs
- 7. Diabetes
  - a. Low dose OCs produce only a mild insulin resistance
  - b. Glucose and insulin levels increase about 1%
  - c. Concern is not with adequate glucose control but with insulin-stimulated atherosclerosis
  - d. Benefits and risks of OC use must be carefully calculated, but OCs may be considered
- 8. Migraine headaches: Women without neurologic signs and symptoms in aura may tolerate OCs
- C. "Interception" or emergency contraceptive pills (ECPs) as a back-up method for barrier method accident, such as condom rupture, diaphragm dislodgement
  - 1. Instruct patient to take 2 Ovral tablets as soon as the accident is recognized and another 2 tablets 12 hours later
  - 2. Therapy will cause a progesterone withdrawal sloughing of endometrium and prevent nidation
  - 3. Only 2 % failure rate calculated if treatment initiated within 48-72 hours

## IX. Other Considerations For Pill Use

Start

- A. Day 1-5 of menses
- B. Immediately after first trimester abortion
- C. 7-14 days after 2nd trimester abortion
- D. 14-21 days after delivery (if breast-feeding, use progestin-only OC until supplemental feeding started)

## X. Noncontraceptive Benefits of OC Use—Summary

- A. Decreased incidence of endometrial and ovarian cancer
- B. Decreased incidence of pelvic inflammatory disease (despite slight increase in cervicitis)
- C. Decreased incidence in benign breast disease
- D. Decreased incidence of functional ovarian cysts (78 % reduction in corpus luteum cysts and 49 % reduction in follicular

cysts)

- E. Decreased incidence of ectopic pregnancy (ectopic pregnancy is the leading cause of maternal morbidity in first trimester)
- F. Decreased menstrual blood loss and decreased anemia
- G. Decreased incidence of fibroids has been suggested:
  - 1. 17 % reduction with 5 years use
  - 2. 50% reduction with 10 years use
- H. Possible reduced incidence of rheumatoid arthritis and increased bone mass
- I. Prevent osteoporosis and other estrogen deficiency problems in women with hypothalamic amenorrhea (stress, dieting, exercise)
- J. Dysmenorrhea control
- K. Eliminate mittelschmerz
- L. Control of symptomatic endometriosis
- M. Reduce acne
- N. Control of menstrual and intraperitoneal ovulatory bleeding in women with blood dyscrasias
- O. Reduce risk of ovarian and endometrial cancer

#### **X. Progestin-only Pill**

- A. Typical failure rates reported in 2-8 % range. Lowest reported failure rate is 1.1%
- B. Has no estrogen and only 35 % of progestin in combination OC
- C. Useful in situation where estrogen is contraindicated or undesirable
  - 1. Breast-feeding patients (particularly before infant is started on supplemental feedings)
  - 2. Patients over 35 with contraindication to combined OC use (smokers)
  - 3. Patients with chloasma
  - 4. Patients with hypertension or history of thromboembolism
  - 5. Patients with migraine headaches
- D. Useful in situations where higher levels of hormones may not be desirable
  - 1. Patient recovering from elevation in transaminase (e.g., S/P mononucleosis)
  - 2. Patients with previous problems with combination OCs (nausea, weight gain)
- E. Useful to help screen patients for long use progestin-only methods (Norplant, Depo-Provera) who have history of possible side effects with OC use
- F. Mechanisms of action
  - 1. Ovulation suppression in 40-60% of cycles
  - 2. Hostile cervical mucus

3. Atrophic endometrium reduces change of successful nidation

G. Drawbacks of method

1. Spotting and amenorrhea
2. Greater chance of method failure than combination OC
3. Greater chance of user failure than combination OC
  - a. Pills must be taken regularly to maintain thick mucus during ovulating cycles
  - b. Missing 1 pill will substantially increase chance of pregnancy
4. Risk of ectopic pregnancy is higher than for users of combination OC pills, but risk not higher than for women using no method
  - a. Decreased tubal motility
  - b. Less suppression of ovulation

I. **Male Condom**

A. Failure rates vary with a number of factors

1. Condoms with spermicide: 10%
2. Condoms alone: 10%
  - a. Unmarried women: 11%
  - b. Married women: 14%
  - c. Women >30 years: 1--4%
  - d. Women <25 years: 10-33%

B. Breakage rates:

1. FDA standards require
  - a. Breakage <4/1000
  - b. Electrical testing for pin holes
  - c. Strength testing by filling with 300 cc H<sub>2</sub>O
  - d. Also some inflation testing with gases
2. 1/161 acts of intercourse
3. Vary with type of intercourse act. For example, the breakage rate is 5.9 % with anal intercourse
4. Increase with lack of lubrication (shearing pressure)
5. Increase with use of petroleum based lubricants (Vaseline, baby oil, vegetable oils, prescription creams like fungicides)
  - a. In tests where condoms were lubricated with these agents, damage occurred within 1 minute
  - b. Within 3 minutes, HIV leaked through 50 % of the condoms
  - c. Water-soluble lubricants or nonoxynol-9 based contraceptive creams avoid this problem
6. Increase with incorrect application
  - a. Placement timing during sex act

- b. Slack left at end of reservoir tip
  - 7. Increase in hot, humid climates
  - 8. Possibly increase with exposure to ozone
- C. Condoms now made in 3 different sizes
  - 1. 160-180 mm in length, 49-52 mm flat width, and 0.04-0.07 mm in thickness
  - 2. Standardization and international specifications are necessary for quality assurance
- D. Noncontraceptive benefits
  - 1. Quite beneficial against diseases infecting areas covered by condom, if condom applied prior to genital contact
    - a. Latex condoms impermeable to organisms: *N. gonorrhoeae*, *C. trachomatis*, *T. pallidum*, HPV, HSV, hepatitis B, and HIV
    - b. Natural membrane condoms more permeable and allow passage of many viruses
    - c. Partners of HIV-infected men who were sexually active
      - (1) 10% HIV conversion rate in the women when condoms were used
      - (2) 86% HIV conversion rate in nonusing couples
    - d. Rates of all STDs markedly reduced
      - (1) Cervical gonorrhea: RR = 0.11--0.97
      - (2) Urethral gonorrhea: RR = 0.34--0.51
      - (3) PID: RR = 0.6
  - 2. Condoms offer protection against many STD sequelae: PID, tubal infertility, cervical dysplasia
  - 3. Thicker condoms blunt sensation and are useful in treatment of premature ejaculation
  - 4. Infertile couple where woman has antisperm antibodies in cervical mucus. Use of condoms drops titers and may permit conception
  - 5. Reported cases of women with serious allergic reactions to sperm
  - 6. Easily accessible, over-the-counter. 600 million-1 billion condoms sold in United States each year
- E. Patient education and motivation key to success
  - 1. Many couples are unfamiliar with application techniques. Educating women to integrate into lovemaking process may have many benefits
  - 2. Dual protection systems may be necessary to protect effectively against pregnancy and STDs
- F. New condoms under development
  - 1. Polyurethane condom
  - 2. Cap condom to cover only glans of penis

## II. Diaphragm

### A. History

1. First described after rubber vulcanization in 1838
2. Popular in 1800s in Europe
3. Introduction into United States in 1916

### B. Types

1. Coil spring
  - a. Rim is round, coiled metal wire
  - b. Good for women with normal pelvic anatomy, no uterine displacement, and deep arch behind pubic symphysis
2. Arching spring
  - a. Rim is double metal spring
  - b. Theoretically preferred in women with poor vaginal support, moderate uterine prolapse and possible anteverted or retroverted cervixes. Usually used interchangeably with coil spring
3. Flat spring
  - a. Rim is fiat metal-bound ring
  - b. Useful when shallow arch behind symphysis

### C. Failure rates vary greatly

1. Typically 18 % per year, with a range of 2-20 %
2. More effective in older women who are having intercourse less than 3x per week and who are well trained in the method

### D. Mechanism of action

1. Cover cervix to prevent sperm entry into upper genital tract
2. Spermicide action localized

### E. Contraindications

1. Allergy to spermicide or latex
2. Woman who can't insert diaphragm herself or have her partner insert it
3. Procidencia

### F. Proper fitting is necessary

1. Sizes: 50-105 mm in diameter in 2.5-5.0 mm increments
2. Ring should fit between posterior aspect of symphysis pubis and extend up into the cul-de-sac
  - a. It should touch both lateral walls and cover the upper vagina and cervix
  - b. The largest size the patient can wear without being aware of it is best
  - c. With orgasm, the upper vagina expands and the diaphragm may become dislodged
3. Patient should be refitted:

- a. Every 2 years
  - b. Anytime she experiences 20% weight change
  - c. After each delivery
  - d. After a 2nd trimester termination
4. Special considerations---suboptimal candidate
- a. Woman with markedly anteverted cervix
  - b. Couple uses female superior coital position
  - c. Woman who has difficulty touching herself or inserting the diaphragm
- G. Proper use and care
- 1. Must be used with spermicide
  - 2. May be placed 2-12 hours prior to coitus
  - 3. Traditional recommendation that additional spermicide be added with each act of intercourse is being reevaluated
  - 4. Careful cleansing and storage techniques optimize efficacy
- H. Side effects
- 1. Increased risk of urinary tract infection due to change in vaginal flora (increased enteric organism count)
    - a. Old hypothesis that diaphragm rim causes urethral obstruction has been disproved
    - b. Clinical studies comparing diaphragm and cervical cap noted increased prevalence of E. coli colonization in the vagina
    - c. New hypothesis: detergent action of spermicide may alter cervical epithelial cells and lead to increased E. coli adherence and colonization
    - d. Only recurrent UTIs are strong relative contraindication to diaphragm use
    - e. Pre- and postcoital urination are useful prophylactic measures
  - 2. Allergic reactions to spermicide and/or latex materials
    - a. Approximately 2-4 % of men and women report local edema, erythema, irritation after exposure to spermicide
    - b. May be mistaken for yeast infection symptoms
  - 3. TSS has been reported with diaphragm but very rarely. Diaphragm should not be used during menses or immediately postpartum
- I. Noncontraceptive benefits
- 1. STD control
    - a. Reduced risk of cervical infections with gonorrhea, chlamydia, syphilis, herpes, HDV
    - b. Questionable data about HIV. Rim of diaphragm may cause micro abrasions permitting entry of virus. The nonoxynol-9 should have significant viricidal effects,

but may also promote transmission.

- c. No protection against vulvar or vaginal infection such as HPV, molluscum, chancroid, etc.
2. Increased rates of PID and STD sequelae
3. Decreased rates of cervical dysplasia

### III. Cervical Cap

- A. Prentif Cavity Rim Cap approved by FDA in 1988. Only type approved for use in United States, although many other designs (Vimule, Dumas) have had long, widespread use in United Kingdom and other European countries
- B. Prentif Cap is shaped like a thimble to cover the cervix
  1. Inner rim fits snugly around cervix
  2. Develops a slight suction to prevent cap dislodgement
- C. Failure rates
  1. 17.4 % overall, range 7-18 %
  2. Method failure: 6.3 %
  3. User failure: 11.1%
  4. Reanalysis of multiparous perfect users showed 26% failure rate
- D. Mechanism of action
  1. Covers cervix to prevent sperm entry into upper genital tract
  2. Spermicide provides extra protection
- E. Proper fitting necessary
  1. 4 sizes available: 22, 25, 28, and 31 mm in diameter
  2. Cervix must be smooth so suction can develop
  3. Check fitting for adequate cervical coverage, proper seal, and positional stability
  4. About 80% of women can be properly fitted
- F. Contraindications to use
  1. History of toxic shock syndrome
  2. Allergy to spermicide
  3. Anatomical variation of cervix which prevents a good fit
  4. Cervical or uterine malignancy
  5. Unresolved abnormal pap smear
  6. Recent cervical biopsy
  7. Acute PID, cervicitis, or vaginal infection
  8. Abortion within 2 weeks
  9. Full-term delivery within 6 weeks
- G. Use
  1. Patient education and practice is essential
  2. Place small amount of spermicide in top of cap and place into vagina
  3. Use for up to 48 hours with no need for reapplication of

spermicide

4. Avoid use during menses

#### H. Follow-up needed

1. Optional recheck after 2 weeks of use to determine whether patient experiences cyclic changes in cervical diameter
2. At 3 month visit
  - a. FDA requires repeat pap smear. Increased dysplasia after 3 months but no differences after 6-12 months
  - b. Ask about partner discomfort
3. After any dislodgement or other problem (postcoital bleeding)

#### I. Side effects

1. Increased risks of urinary tract infection
2. Women's allergic reaction to spermicide. Partners are rarely exposed to spermicide
3. No reported cases of TSS, although potential is present. Avoid using cap during menses or post partum
4. Vaginal odor if left in too long
5. Discoloration and odor if device is not properly cleansed

#### J. Advantages

1. Convenient, not messy, long wear, spontaneity permitted
2. STD protection against cervical infections such as chlamydia and gonorrhea. Questions about risk of increased HIV vulnerability when cervical tissue is traumatized. Spermicide may reduce or increase the risk
3. Reduce risks with STD sequelae, such as PID, tubal infertility, and cervical dysplasia

### IV. Vaginal Spermicides

#### A. Nonoxynol-9 and octoxynol-9

#### B. Types

1. Melting and foaming suppositories---should be inserted 15-30 minutes prior to intercourse
2. Foaming tablets--require 15 minutes to activate
3. Aerosol foams-instantly spermicidal
4. Gels--need to wait until materials reach body temperature for complete effectiveness
5. Creams- restriction as gels
6. Soluble films (VC) restriction as gels

#### C. Mechanisms of action

1. All forms are surfactants and detergents, which attack the acrosomal membranes, destroying them or rendering the sperm immotile
2. All spermicides are delivered in a base which covers the cervix to some degree

D. Failure rates

1. Typical: 21%, range: 3-31
2. Motivation and usage factors are important

E. Use

1. Allow time for activation
2. Correctly timed intercourse
3. Additional applications needed for multiple acts of

intercourse

4. No douching for 6 hours postcoitus

F. Advantages

1. Easily obtained, over-the-counter
2. Relatively low cost
3. Provides some protection against both bacterial and viral STDs. Inhibits growth of *N. gonorrhoea*, *C. trachomatis*, HSV-2, *Trichomonas vaginalis*, *Treponema pallidum*, and HIV. (Detergent action of spermicide may make patient more susceptible to infection if exposed to HIV or hepatitis B)
4. Local activity, no systemic reactions (although distributed throughout body)

G. Disadvantages

1. Interrupt sex to apply
2. Messy or difficult to apply
3. Unpleasant smell or taste
4. Allergic reaction in 2-4 % of men and women

H. Previous concerns about potential teratogenicity of these formulations have been scientifically disproved

V. Female Condoms Reality

- A. Designed to provide protection against vaginal and sometimes perineal and vulvar STDs
- B. Diaphragm-like, polyurethane covering for cervix within sheath extending to introitus
- C. Covers the vagina, cervix, and base of the penis
- D. Spermicide added prior to intercourse
- E. Pregnancy rate: 12/100 women years
- F. Long-term patient acceptance questioned in clinical trials