

HORMONAL CONTRACEPTION

The RxFiles

January, 2000

HIGHLIGHTS

- ◆ **Current low dose OCs are highly effective with an excellent safety profile and many associated health benefits**
- ◆ **No single product has been shown to be superior in efficacy, safety or tolerability**
- ◆ **There is no "one size fits all" OC; different women may require different formulations**
- ◆ **Smoking particularly after age 35 with concurrent OC use greatly increases cardiovascular and thrombotic risks**
- ◆ **Age alone is not a significant risk and OCs are considered safe for use in women up to the age of menopause**

ORAL CONTRACEPTIVES:

Since their introduction in the 1960s, oral contraceptives (OCs) have grown in number and popularity. In America, 30% of women of reproductive age use OCs and up to 80% of all women will use OCs at some time in their life.¹

Current status: The first OCs of the 1960-70's contained 50-100 ug of estrogen along with 1-10mg of progestin. Cardiovascular complications (MI, thrombosis, and stroke) and increased incidence of breast, uterine, and cervical cancer limited their usefulness. In the mid '70's several lower dose estrogen pills were introduced. Hormone content was further reduced with the development of bi- and triphasic formulations which also attempted to more closely mimic the natural menstrual cycle. The latest progress has been the emergence of a new generation of progestins aimed at reducing androgenicity, hypertension, and cardiovascular risk. A combination contraceptive patch may soon be available as well.

Currently in Canada, over 20 products are available. Products vary in the amount and type of estrogen and progestin, and in their phasic nature. Monophasic OCs contain a fixed amount of estrogen and progestin throughout the entire cycle. Biphasics contain a fixed amount of estrogen while the progestin content increases in the second half of the cycle. Triphasics may have a fixed or variable amount of estrogen along with a dosage of progestin that varies in 3 phases.

Comparative Efficacy: Ethinyl estradiol (EE) and mestranol are the two types of estrogen used in OCs. Mestranol is a prodrug that is converted to estradiol in vivo; 50 ug is equivalent to 35 ug of estradiol. OCs contain 1 of 7 different progestins. All are 19-nortestosterone derivatives including the third generation desogestrel and norgestimate (further derivatives of levo-norgestrel). Much is made of the estrogenic, anti-estrogenic, progestogenic, and androgenic differences between these agents. The clinical significance of

these differences is unclear as much of the data is based on animal studies which are not readily extrapolated to humans. Well designed comparative trials between products are lacking.²

Despite the dose reduction OCs have undergone in recent years, they remain among the most effective, reversible methods of contraception available. The pill is said to be 99.9% effective although the typical user failure rate is about 3% per year.³ Efficacy is compromised by missed or delayed doses (Table 7), drug interactions (Table 6), illness affecting GI absorption (vomiting, diarrhea, inflammatory bowel disease) and other patient variables (eg. smoking). In some cases a back-up or alternate method of contraception should be used.

Besides the advantages of simplicity, reversibility, and excellent efficacy, OCs confer many other health benefits. Patients and sometimes practitioners often overlook the improvements in the menstrual cycle and reduction in certain disease and cancer incidence associated with use of OCs (Table 2).

Comparative Safety: All of the current OCs in Canada contain 50 ug or less of estrogen. This has significantly improved their safety profile without compromising efficacy. Despite many health benefits, use of OCs is not without risks (Table 4). Although increased rates of breast and cervical cancer are reported among OC users, it is unclear whether there is a causal relationship due to the presence of other related, confounding factors (eg. delay of childbearing, early sexual activity, number of partners, etc).

Arterial and venous thromboembolic events are increased, particularly in women >35 years old who smoke and in those with known risk factors (hypertension, diabetes, obesity). The new progestins were specifically developed with a view to improving cardiovascular safety. Trial results have been variable and interpretation controversial.⁵ Although the new progestins may produce beneficial changes in the lipid profile compared to previous progestins, this may not be of great advantage. Cardiovascular events in OC users are thrombotic not athero-sclerotic in origin and no study has shown an increase in MI rates among OC users who do not smoke or have other risk factors.⁴ Since the net change in lipids appears to be of minimal clinical significance and unlikely to adversely affect cardiovascular risk, all low-dose OCs are considered lipid neutral and antiatherogenic regardless of the progestin's effect on the lipid profile.⁴ The risk of clotting appears to be increased a further two fold with the new progestins compared to other low-dose OCs but whether this is a direct effect or some type of predisposition in 1st time users remains unclear.⁵

Smoking especially in women over 35 years old significantly increases the risk of cardiovascular disease, stroke and acute MI. OC use further compounds the harmful effects of smoking. Age alone is not a significant risk and OCs are now considered safe for long term use in women up to the age of menopause provided they have no other major risk factors.² Women using nicotine gum or patches or those exposed to second hand smoke have the same risk as those who actually smoke.⁶ Smokers should be encouraged to quit or to use an alternate method of contraception. When this is not possible, OCs with 20ug EE can be prescribed cautiously if cigarette consumption is limited to <15 cigarettes/day.⁶

OCs may exacerbate certain disease states:

- **cholelithiasis** due to increased cholic acid secretion and greater gallstone formation
- **diabetes** due to peripheral insulin resistance and impaired glucose metabolism although OCs with ≤ 35 ug EE have no appreciable effect on carbohydrate metabolism⁷
- **hypertension** due to sodium and water retention and increased renin activity although current low dose OCs rarely cause clinically significant increases in BP.⁸
- **hyperlipidemia** due to increased triglycerides related to estrogen content and reduced HDL due to the effect of the progestin; although OCs containing the new progestins have the most favorable lipid profile, today's low dose OCs are all considered antiatherogenic.

Side effects: Only 1/2 - 2/3 of women who start OCs are still using them after 1 year.⁹ Adolescents have a reported 50% discontinuation rate within the first 3 months of use.¹⁰ While the reasons are many and often unknown, in one recent study 59% of women cited side effects as the most common reason for stopping OCs (excluding women desiring pregnancy or no longer in a sexual relationship).¹¹ Bleeding irregularities were most common followed by nausea, weight gain, mood change, headache, and breast tenderness. Although related to hormone content and balance, many of these side effects are transient often resolving within the first 3 cycles. Effects that persist beyond this may require a change to another OC with a different hormone composition (Comparative Chart).

Switching within the first 3 months is usually not necessary due to the self-limiting nature of many initial symptoms.

Management of side effects is discussed in Table 5.

Adequately counseling patients about the occurrence, transiency, and management of common side effects can significantly improve compliance rates.¹²

Much of the reported difference in androgenicity between older and newer progestins is based on animal studies using supraphysiologic doses. In the contraceptive doses used, none of the current progestins can be considered androgenic. In fact all combination OCs (COCs) are considered anti-androgenic due to the influence of estrogen. They are all beneficial in treatment of hirsutism and acne.¹³

Choosing an OC

Since well-controlled comparative trials are lacking, no product has been shown to be of superior efficacy or tolerability.² Unfortunately, choosing an OC is more of an art than a science. For most young healthy women without co-morbid disease, contraindications, or major risk factors, **an OC with the lowest effective hormone dose should be prescribed initially for a trial of 3 months** (eg. ≤ 35 ug EE and ≤ 1 mg norethindrone, ≤ 0.25 mg norgestimate, or ≤ 0.15 mg desogestrel or levonorgestrel).¹⁴

Although the monophasics are thought to have better cycle control with less breakthrough bleeding (BTB) than the

triphasics, **by the 4th cycle all products are basically equivalent regardless of phasic formulation or progestin content.**¹⁵ Smoking and delayed or missed doses probably have a more significant impact on BTB than product formulation.¹⁵

Compliance and overall efficacy can be enhanced by providing adequate instruction on the importance of establishing a regular pill-taking routine, proper initiation of OCs (Table 3), managing missed doses (Table 7), occurrence and management of common side effects, early danger signs (ACHES - Table 4), and the possibility and management of drug interactions (Table 6) including use of backup methods of contraception.

The "Morning After Pill" (MAP)

The MAP provides emergency post-coital contraception (EPC) when given within 72 hrs of unprotected intercourse occurring around the time of ovulation. The probability of pregnancy approaches zero if intercourse occurs more than 2 days after ovulation.¹⁶ Unfortunately ovulation status is rarely known precisely. High doses of estrogen and progestin are given to delay or prevent ovulation, impair sperm and ova transport, and cause sloughing of the endometrial lining to prevent implantation of the fertilized ovum. For maximum efficacy, MAP should be given within 72 hrs after unprotected sex, and ideally within the first 24 hrs. After 72 hrs the efficacy of MAP rapidly declines and it is ineffective by 7 days. This method (Yuzpe) results in a 75% reduction in the number of pregnancies that would occur if no EPC were used.²

Ovral® is considered the pill of choice because of its low failure rate (<2%) and reduced risk of nausea and vomiting.¹⁷ 2 pills are taken immediately followed by 2 pills 12 hrs later; alternately 2 pills OD x 2 days can be given particularly if pills would otherwise have to be taken in the evening or night hours or when nausea with vomiting is likely. Preven®, a kit containing the 4 required tablets as well as a pregnancy test is now on the market; the kit costs \$33 compared to \$22 for Ovral®. If Ovral® or Preven® are unavailable, 4 OC pills (containing ≥ 35 ug EE each) can be used for each dose.²

Nausea occurs in 50% of women and vomiting in up to 20%.¹⁸ Doses vomited within 1 hr of ingestion must be repeated. Prophylactic antiemetics can be given prophylactically with each dose (eg. dimenhydrinate GRAVOL® 50mg). Other side effects include cramping, spotting, and breast tenderness. Patients should be advised to contact their doctor if they have severe abdominal pain, chest pain, headache, eye problems or leg pain.

Patients should be seen 1 week later for follow-up and again in 3-6wks; if little or no bleeding occurs after 21 days, a pregnancy test should be done. MAP failure rates range from 0-2.4% (i.e. 98% of women will menstruate within 21 days).² Reliable data on the outcome of resultant pregnancies is lacking but given the safety of OCs, teratogenicity is not likely.¹⁹

The MAP remains a controversial ethical issue since some view the method as abortive rather than contraceptive. The SOGC and many women's health groups advocate greater use and availability with the aim of reducing the number of unwanted pregnancies and abortions. Others have concerns regarding the potential abortive mechanism, associated risks and abuse potential.

The Rx Files: Oral Contraceptives - Supplementary Tables

Table 1: Contraindications and Precautions²

Contraindications:

- ◆ active thromboembolic disease
- ◆ undiagnosed vaginal bleeding
- ◆ acute or chronic obstructive liver disease
- ◆ known or suspected breast cancer
- ◆ known or suspected pregnancy

Precautions :

- ◆ **Hypertension** - can use Ocs if hypertension controlled
- ◆ **CVD, hyperlipidemia**- OCs with new progestins preferred because of more favorable lipid profile
- ◆ **Diabetes** - low dose OCs unlikely to affect glucose control but estrogen may complicate vascular disease
- ◆ **Epilepsy** - some anticonvulsants ↓ OCs efficacy due to ↑ metabolism; may require use of OCs with >35ug EE
- ◆ **Hepatitis, cirrhosis** - avoid OCs if active disease; may use if liver enzymes have returned to normal
- ◆ **Gallbladder disease** - may be exacerbated by OCs
- ◆ **Migraine** - avoid OCs if classic or complex (↑ risk of stroke)
- ◆ **Inflammatory bowel disease** - active diarrhea may reduce absorption and efficacy of OCs and require backup method
- ◆ **Systemic lupus erythematosus** - avoid OCs as estrogens can complicate vascular disease
- ◆ **Smoking women** over age 35 - if light smoker (<15cigs/day) or on nicotine patch, can use 20 ug EE product with caution

Table 3: Starting Hormonal Contraceptives

Starting Combined OCs:

- ◆ **most effective if started Day 1 of menstrual period**
- ◆ can be started any day up to Day 6
- ◆ to avoid wknd periods, start on first Sunday after period begins
- ◆ **if started after Day 5 use backup method for first 7 -10 days** as ovulation may not be suppressed

Starting Progestin-only Pill (POP):

- ◆ start on Day 1 of menstrual period and daily thereafter
- ◆ use backup method for first month

Starting Depo-Provera®:

- ◆ should be injected during the first 5 days of menstrual cycle to rule out pregnancy
- ◆ repeat injection q3months (12 weeks) - effective for up to 14 wks

Starting Norplant®:

- ◆ insert within the first 7 days of menstrual cycle to rule out pregnancy
- ◆ must be removed and replaced after 5 yrs

Table 4: ACHES - OCs Early Danger Signs²⁰

SIGN	PROBLEM
Abdominal pain (severe)	Gallbladder disease, pancreatitis, hepatic adenoma, thrombosis
Chest pain (severe), SOB	Pulmonary embolus or acute MI
Headaches (severe)	Stroke, hypertension, migraine
Eye problems - blurred vision, flashing lights, blindness	Stroke, hypertension, vascular insufficiency
Severe leg pain (calf or thigh)	Deep vein thrombosis (DVT)

Table 2: Benefits & Risks^{2, 30}

Benefits:

- ◆ Simple and highly effective
- ◆ Reduces need for sterilization & abortion
- ◆ **Significantly improves menstrual symptoms & regularity**
 - ◆ Reduces dysmenorrhea and mittelschmerz
 - ◆ Reduces menstrual blood loss (up to 50%)
 - ◆ Reduces risk of anemia
 - ◆ Reduces PMS
 - ◆ Alleviates menorrhagia/hot flashes in perimenopausal ♀
- ◆ **Decreases incidence of disease**
 - ◆ bacterial pelvic inflammatory disease (60%)
 - ◆ ectopic pregnancy
 - ◆ endometriosis
 - ◆ *endometrial cancer (>50%)
 - ◆ *ovarian cancer (>40%)
 - ◆ ovarian cysts (>60%)
 - ◆ acne and hirsutism
 - ◆ fibrocystic breast disease (50-75%)
 - ◆ osteoporosis
 - ◆ rheumatoid arthritis (50%)

* benefit greatest with long term use (>5yr) and persists up to 15 yrs after discontinuing

Risks:

- ◆ **venous thromboembolism** = ↑ 3-4x with low dose OCs and further ↑ 2x with new progestins (estrogens ↓ activation of Protein C so ↑ risk of thrombus)^{21,22,23}
- ◆ **arterial thrombosis** (myocardial infarction and stroke) - related to estrogen dose ≥50 ug, age >35, smoking, hypertension, and other risk factors for CVD (↑~2-3x); otherwise no ↑ risk over baseline in young non-smoking ♀²⁴
- ◆ **breast cancer** = ↑ 1.5x; women who started OCs at early age for long duration at greatest risk; persists for 10yrs after d/c²⁵ (also related to nulliparity/delay in childbearing)
- ◆ **cervical cancer** = ↑ 1.5x with long term use (>5yr)²⁶; also related to early sexual activity & multiple partners
- ◆ **gall bladder disease** = ↑ 1.5x during 1st 5yrs of OC use
 - ◆ does not protect against STDs
 - ◆ may exacerbate and/or precipitate: hypertension, diabetes, gallbladder and liver disease, SLE, migraine headaches, depression, GERD, vaginal yeast infections

Table 5: Side Effects and Their Management^{2, 27}

- ◆ **Breakthru bleeding** - most common in 1st 3 months; if persists beyond 3-6mon check for other causes (eg. chlamydia). Change to OC with ↑ estrogen/progestin depending on when BTB occurs in the cycle; may also be related to poor compliance, smoking, DIs
- ◆ **Breast tenderness** - if persists beyond 1st 3months rule out pathologic causes; change to OC with ↓ estrogen/progestin
- ◆ **Weight gain** - may cause ↑ appetite in 1st month but overall weight gain is minimal with low dose OCs and within normal limits for age-related gain; may be cyclical due to Na & H2O retention
- ◆ **Nausea** - often subsides within 3 months; take at hs with food or change to lower estrogen content
- ◆ **Headache** - tension headaches unaffected but hormone related or vascular migraines may ↑↓; if precipitated or exacerbated by OCs should avoid their use
- ◆ **Acne** - sometimes worsens initially but usually improves in the longterm; change to ↓ androgenic OC or use topical therapy
- ◆ **Chloasma** - irreversible and idiosyncratic; exacerbated by sunlight so use sunscreen and reduce exposure; ↓ estrogen dose

Table 6: Drug Interactions²⁸⁻²²

AGENT	EFFECT AND MECHANISM	MANAGEMENT
*Anticonvulsants: Carbamazepine Ethosuximide Barbiturates Primidone Phenytoin	↓ OCs efficacy due to ↑ hepatic metabolism ↑ phenytoin conc. due to ↓ metabolism	Use OCs with 50 ug EE Change to alternate anticonvulsant Use alternate method of birth control (BC) Monitor serum phenytoin and ↓ dose prn
*Antibiotics: Penicillins (esp. ampi) Cephalosporins Macrolides Metronidazole Sulfas/Cotrimoxazole Tetracycline Rifampin	↓ OCs efficacy due to ↑ intestinal transport (diarrhea) and ↓ enterohepatic reabsorption of estrogen ♦interaction with rifampin most significant! ↓ OCs efficacy due to ↑ metabolism	Estimated failure rate is approximately 1% per year Likely subgroup at ↑ risk due to dependence on enterohepatic reabsorption but unable to identify these ♀ so counsel all If long term treatment, use alternate method of BC; if short term, use back-up method of BC for that cycle Management as above for either long-term or short term
Antifungals: *Griseofulvin	↓ OCs efficacy due to ↑ metabolism	Management as above
Benzodiazepines: Alprazolam, Chlordiazepoxide, Diazepam, Nitrazepam, Triazolam Oxazepam, Lorazepam, Temazepam	↑ benzodiazepine conc. due to ↓ oxidative metabolism ↓ benzodiazepine conc. due to ↑ glucuronidative metabolism	Monitor for ↑ side effects and possible toxicity; reduce dose prn Monitor for loss of benzodiazepine effect and ↑ dose if needed
*Corticosteroids	↑ steroid conc. due to ↓ metabolism	Monitor for side effects and toxicity; reduce dose as needed
*Cyclosporin	↑ cyclosporin conc. due to ↓ metabolism	Monitor for side effects and toxicity and reduce dose as needed
Grapefruit juice	↑ estrogen levels due to ↓ metabolism	Monitor for side effects and switch to lower dose EE if needed May consider avoiding grapefruit juice; orange juice OK
Insulin and Hypoglycemics	OCs with 50 ug EE may impair glucose tolerance in predisposed women	Use OCs with 35 ug or less EE; monitor blood sugars and ↑ dose of insulin or hypoglycemic; Use alternate method of BC
Imipramine Clomipramine	↑ TCA conc. due to ↓ metabolism	Monitor for side effects and toxicity and reduce dose prn
Theophylline	OCs with ≥ 35 ug EE may ↑ theophylline conc. due to ↓ metabolism	Monitor theophylline levels and reduce dose prn Use OCs with < 35 ug EE
Thyroid	↓ levels of free thyroxine due to estrogen - induced ↑ in thyroxine binding globulin	May need to ↑ dose
*Warfarin	OCs ↑ risk of thromboembolism and may ↑↓ anticoagulant effect due to changes in metabolism	Avoid OCs and use alternate method of contraception Monitor PT times and adjust dose esp. if OCs started, stopped, or changed (brand, dose, etc)

* of greatest clinical significance; (probably <5% of drug interactions with OCs results in pregnancy²⁹)

Table 7: Management of Missed Doses

<ul style="list-style-type: none"> • #1 compliance problem especially if no set routine so should try to associate with some activity of daily living (eg. hs) • risk of pregnancy greatest if pills started late or missed at the beginning or very end of a cycle • a single missed dose of little consequence if remembered within the window of opportunity (12-24 hrs after last dose) • CHECK WITH PHYSICIAN IF 2 MENSTRUAL PERIODS ARE MISSED IN A ROW 	
<p style="text-align: center;">SOGC Guidelines (for 21 day pill packs)²</p> <p>Miss 1 pill: Take it now and take subsequent pills as usual</p> <p>Miss 2 pills in a row:</p> <ul style="list-style-type: none"> ♦1st 2 weeks: Take 2 pills now and 2 pills the next day Take subsequent pills as usual Use backup method for the 7 days following missed pills ♦3rd week*: Discard remainder of pill pack and start new pack that same day Use backup method for the next 7 days May not have a period this month <p>Miss 3 pills in a row*: Discard remainder of pill pack and start new pack that same day; Use backup method for the next 7 days May not have a period this month</p> <p>* Sunday starters should continue taking 1 pill daily until Sunday and then follow instructions as above</p>	<p style="text-align: center;">International Planned Parenthood Federation Guidelines: (for 21-day pill packs)¹⁹</p> <p>How long since last pill taken??</p> <p>12 hours or less: Take missed pill now Take subsequent pills as usual</p> <p>More than 12 hours: Take missed pill now Discard any other missed pills Use backup method for next 7 days If >7 pills left, finish package as usual and start new one 7 days later as usual If < 7 pills left, finish package as usual but start a new one the next day (no pill free break) - may not have a period this month</p>

PROGESTIN ONLY PRODUCTS

The Progestin-only-pill (POP), also called the "minipill", is indicated for use in women in whom estrogen is contraindicated or intolerable, who have a history of VTE or migraine, are post-partum or lactating, or who smoke. The only contraindications are pregnancy and undiagnosed vaginal bleeding. **Micronor®** (norethindrone 0.35 mg) is the only POP currently available in Canada.

The POP inhibits ovulation in only 60% of women so relies on endometrial and cervical mucus changes for its contraceptive effect. Compared to COCs, efficacy is somewhat lower at 90-99%.² Cervical permeability diminishes within 22hrs of ingestion and is unimpaired by 24hrs.³⁰ Hence compliance is more critical as **the pills must be taken at the same time each day within 3 hrs for reliable effect.** POP should be started on day 1 of the menstrual cycle and continued daily thereafter with no pill-free days. A backup method of contraception is required for the first month. If a pill is missed or delayed, it should be taken immediately and a backup method used for the next 48hrs; if 2 pills are missed, 2 pills should be taken stat, followed by 2 the next day and a backup method used till the next menstrual period. If no period occurs within 45 days, test for pregnancy.

Due to the absence of estrogen and the reduced progestin content (about 1/2-2/3 that of COCs), side effects with POP are substantially reduced. Menstrual disturbances are the most common problem and patients should be so advised. Persistent abnormal bleeding should be investigated to rule out pathological causes; if prolonged amenorrhea occurs, pregnancy status should be evaluated. Ovarian cysts and ectopic pregnancy may also occur infrequently.

Long-acting Progesterone depot injection (Depo-Provera®) is a simple, well-tolerated and extremely reliable method with a failure rate of < 0.3%.² The sustained levels of medroxyprogesterone (MPA) suppress ovulation, induce endometrial atrophy and make cervical mucus impermeable to sperm.

Depo-Provera® is the only preparation available in Canada; 1ml of 150mg MPA in a slow-release vehicle is given by deep IM injection every 3 months. The initial dose should be injected in the first 5 days of the menstrual cycle to avoid inadvertent administration during early pregnancy. Appointments for repeat injections should be made at **~12 week intervals** although studies show the dose is effective **for up to 14 weeks.**³¹ If repeat injection is late, one must test to ensure that the patient is not pregnant prior to giving the next injection. Indications are similar to POP but not exclusive of women simply desiring this method for convenience; the only contraindications are pregnancy and undiagnosed vaginal bleeding.

Advantages include:^{2, 32}

- ♦ scanty menses or amenorrhea (50% of women after 1yr)
- ♦ prevention of anemia
- ♦ reduction in PMS, dysmenorrhea, endometriosis
- ♦ less pelvic inflammatory disease
- ♦ reduced risk of endometrial and cervical cancers
- ♦ reduced seizure frequency

Drawbacks include:^{2, 32}

- ♦ menstrual cycle disturbance
- ♦ weight gain of an average of 1-2 kg/yr (reversible)
- ♦ decreased bone density related to dose and duration (reversible)³³
- ♦ delay in return of ovulation (average = 8 months but may take up to 2yrs)
- ♦ headache, mood changes, lethargy, mastalgia, bloating, acne

Progestin Implant (Norplant®) provides the most effective method of hormonal contraception with a failure rate of <0.2%.² Unlike depot injections, problems with patient compliance are eliminated once the device is inserted and reliable contraception is provided for up to 5 years. Indications and contraindication are similar to the other progestin-only products.

Norplant® is the only implant available in Canada. It consists of 6 rods containing a total of 36 mg of levonorgestrel which are inserted subdermally on the medial aspect of the upper arm. The rods slowly release the levonorgestrel which inhibits ovulation, induces endometrial atrophy, and makes cervical mucus impermeable to sperm. The device should be inserted within the first few days of the menstrual cycle and is effective within 24hrs. **Disadvantages include:**²

- ♦ high initial cost - > \$500 plus cost of insertion and removal
- ♦ need for surgical insertion and removal
- ♦ menstrual cycle disturbance (>85 % of users)
- ♦ weight gain
- ♦ reductions in HDL (significance unclear)
- ♦ ovarian cysts
- ♦ headache, depression, mastalgia, acne

PROGESTIN PRODUCTS - COMPARATIVE COSTS:

PRODUCT:	COST PER YEAR:
Micronor® (13 packs)	\$ 230
Depo-Provera® (4 injections)	\$ 150
Norplant® (per year)	\$ 110
Norplant® (total cost for 5 yrs)	(\$ 515)

Cost per year based on approximate retail cost to consumer in SK (including markup & dispensing fee).

References available on request.

The material in this newsletter topic area is subject to some ethical controversy. Information included has been given upon physician request and does not necessarily reflect the ethical views of the writers, reviewers, or Saskatoon District Health.

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Sharon Downey BSP, Loren D. Regier BA, BSP

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