

Hormonal Contraception DEPO-PROVERA

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A. General Considerations

- Depo-Provera (depot-medroxyprogesterone acetate) is a long-acting injectable contraceptive
- Currently the only injectable contraception in the U.S.
- Widely used for 30 years world-wide; lots of data
- Extremely low failure rate, 0.3%
- Cost is acceptable (\$42.20/injection for students at USHS)
- Ideal choice if estrogen contraindicated as form of contraception
- First dose in the first 5 days of menses
- Gaining in popularity among teenagers as well as adults
- May be used to manage other gynecologic problems such as fibroids
- Extensive pre-use counseling required as the drug is long-acting
 - ◆ Patients should be aware that once given, Depo-Provera cannot be neutralized or reversed if side-effects are experienced
 - ◆ Patients should receive written educational material about the drug and should be allowed time to study the material before administering the injection
 - ◆ Patients should sign a consent form prior to giving the injection (USHS policy)
- Patient information is available at www.depoprovera.com Company also provides email reminders for repeat injections.

B. Mechanism of Action

- Suppresses ovulation
- Thickens cervical mucus
- Creates a thin, atrophic endometrium

C. Indications

- Safe for women in good health and who do not have absolute contraindications
- Appropriate for women who:
 - ◆ Want long-term continuous contraception

- ◆ Want to avoid coitus-dependent methods of contraception
- ◆ Want to avoid a contraceptive method which requires a daily regimen
- ◆ Cannot tolerate estrogen-containing methods
- ◆ Need a contraceptive that does not increase the risk of thrombosis
- ◆ Are breastfeeding (do not give first injection until 6 weeks post-partum)
- ◆ Are taking anticonvulsants or rifampin or other drugs which decrease the efficacy of combined oral contraceptives

D. Contraindications

Absolute Contraindications:

- Known or suspected pregnancy
- Undiagnosed vaginal bleeding
- Known or suspected breast or genital malignancy or hormone dependency malignancy
- Known sensitivity to depot-medroxyprogesterone acetate or any of its ingredients
- History of severe endogenous depression

Relative Contraindications (This means that individual assessment and management are required; not that you can't use Depo in these patients)

- History of MI or CVA
- HTN
- Hyperlipidemia
- Diabetes mellitus
- Migraine headaches
- History of thromboembolic disease

E. Other Considerations

- May cause fluid retention so conditions that may be influenced by fluid retention such as epilepsy, migraines, asthma, and cardiac or renal dysfunction require more careful observation
- Decreased glucose tolerance has been observed in some patients so those with diabetes should be monitored
- Patients desiring pregnancy within a year should carefully consider before choosing Depo-Provera as it is long-lasting and there may be a delay up to 10-13 months in return of fertility following the last injection.
- Patients who dislike injections or who are unable to receive injections every three months should consider another option

- Patients uncomfortable with irregular bleeding or amenorrhea should not receive Depo-Provera

F. Noncontraceptive Benefits

- Reduces the risk of endometrial cancer during and for several years following the discontinuation of Depo-Provera
- Reduces the incidence of iron-deficiency anemia
- Possibly decreases the risk of PID
- Reduces the incidence of ectopic pregnancies
- May be especially useful for women with endometriosis, dysmenorrhea, menorrhagia or uterine fibroids
- Reduction in epileptic attacks, aggression and mood swings, especially useful in mentally handicapped patients
- Lactation not suppressed
- Patients have one week grace period

G. Side-Effects

- **Menstrual changes** consist of irregular or unpredictable bleeding or spotting, and amenorrhea.
 - ◆ Advise women that they possibly may need to wear a pad or tampon daily for the first 6 months.
 - ◆ By the end of year one, 57% of women will be amenorrheic
 - ◆ By the end of year two, 68% will be amenorrheic
- **Weight gain** is predictable and more than 70% of women will gain weight!:
 - ◆ 5.4 lbs on average the first year
 - ◆ 8.1 lbs after two years of use
 - ◆ 13.8 lbs after 4 years of use
 - ◆ 16 lbs by year 5
- **Decrease in bone density**
 - ◆ Estrogen levels decrease to 20 pg/ml range with continued use.
 - ◆ Early studies by Cundy^{1,2} showed significantly lower mean lumbar bone density in women who had used Depo-Provera for at least 5 years; the bone loss was reversible upon discontinuation of the drug.
 - ◆ Cromer³ published a 2 year prospective study examining bone density changes in adolescents comparing patients receiving hormonal contraceptives with a control

¹ Cundy, et.al. *British Medical Journal*, 1991;303:13.

² Cundy, et.al. Recovery of bone density in women who stop using medroxyprogesterone acetate, *British Medical Journal*, 1993; 308:220.

³ Cromer, BA, et.al. A prospective comparison of bone density in adolescent girls on depot medroxyprogesterone acetate (DMPA, Norplant or OC's), *J.Peds*, 1996; 129:67-76

arm. The bone density decreased by 3.1% at two years in the Depo-Provera group compared with a 9.5% increase in the OC users.

- ◆ Other studies have shown that bone-density decreases only slightly in long-term Depo users.^{4,5} Long-term follow-up after Depo use showed that former-users had similar bone densities to never-users.
- ◆ A good review of the various bone studies is presented in the Bigrigg reference.
- **Other side-effects:**
 - ◆ Headache
 - ◆ Nervousness
 - ◆ Breast discomfort
 - ◆ Abdominal pain or discomfort
 - ◆ Dizziness
 - ◆ Weakness or fatigue
 - ◆ Decreased libido
 - ◆ Backache
 - ◆ Leg cramps
 - ◆ Depression
 - ◆ Pain at the injection site
 - ◆ Hair loss
 - ◆ Acne

H. Drug Interactions

- The only drug that may diminish the effectiveness of Depo-Provera is aminoglutethimide (Cytadren), a drug which is used to suppress adrenal function in selected cases of Cushings

I. Management of Patients on Depo-Provera

- Complete physical with pelvic examination and Pap smear
- LFT's indicated if history of liver disease
- Patient should sign informed consent after receiving counseling about effectiveness, side-effects and risks vs benefits. All questions should be answered before the consent is signed. Warning signs should be reviewed and the patient instructed to call the clinic immediately if the following should occur:
 - ◆ Sharp chest pain, coughing up blood, or sudden shortness of breath
 - ◆ Sudden severe headache or vomiting, dizziness or fainting, problems with eyesight (blurred vision/double vision/loss of vision) or speech; weakness or numbness in an arm or leg
 - ◆ Severe pain or swelling in the calf

⁴ Tang OS et al. Further evaluation on long-term depot-medroxyprogesterone acetate use and bone mineral density: a longitudinal cohort study. *Contraception*, 2000;62:161-164.

⁵ Petitti DB et al. Steroid hormone contraception and bone mineral density: a cross-sectional study in an international population. *Obstet Gynecol* 2000;95:736-744

- ◆ Unusual heavy vaginal bleeding
- ◆ Severe pain, or tenderness in lower abdomen
- ◆ Persistent pain, bleeding or pus at the injection site
- ◆ Any concern about possible pregnancy
- The patient must have a negative urine pregnancy test before receiving the first injection of Depo-Provera (USHS policy)
- If the patient is receiving her first injection of Depo-Provera, it should be given during the first 5 days of a normal menstrual period (no barrier method of contraception need be used under these circumstances) The patient should be questioned about the date of last intercourse and contraceptive method used. If there is any doubt about possible pregnancy even with a negative urine pregnancy test, have the patient return after abstaining from intercourse for 2 weeks. Repeat the urine pregnancy test at that time and if negative, then Depo-Provera may be administered. Be aware that giving Depo-Provera at any other time in the menstrual cycle except during the first 5 days may increase irregular bleeding.
- Depo-Provera may also be given under the following circumstances:
 - ◆ Immediately (within 5 days) post-abortion or post-partum, unless breastfeeding in which case the injection should be given 6 weeks post-partum (this is to allow for the infant's liver to achieve sufficient enzymes levels to process exogenous hormones in breast milk, although there is no evidence of an effect)
 - ◆ If the patient is on a highly reliable method of birth control (OC's, Norplant or IUD), she may receive the injection at any time. If she is on OC's, she should continue to take them until the end of her current cycle. If she is using Norplant, she should wait two weeks after the injection to have the Norplant removed.
- Instruct the patient to return in 12 weeks for repeat injection. There is only a 1 week grace period. It is acceptable to give the repeat injection of Depo-Provera during week 12 or 13 or up to 90 days from the last injection. If the patient is later than 90 days, she should be treated as though she were starting Depo-Provera for the first time. Early injection does no harm but late injection increases the risk of pregnancy.
- A pre-filled syringe or a single dose vial containing one ml of 150 mg Depo-Provera should be used. The vial must be vigorously shaken just before use to ensure a uniform suspension.
- Injections can be administered with a 23 or 25 gauge needle, 1 ½ inches long. Give a deep intramuscular injection. It must penetrate the gluteal or deltoid muscle (gluteal is the recommended site). If not given intramuscularly, it may not have consistent absorption. Do not massage site after giving, as this can accelerate absorption.
- At follow-up visits, the clinician should update the history with documentation of bleeding patterns and other side-effects, and check the BP. If the patient is late for the injection (beyond 90 days), she should be treated as though she were starting Depo-Provera for the first time. Emergency contraception should be offered if unprotected intercourse occurred in the past 72 hrs. If the patient received their last injection on-time elsewhere, and this can be documented, a urine pregnancy test need not be done.

J. Discontinuing Depo-Provera

- Instruct the patient to discontinue Depo-Provera 9 months before attempting pregnancy
- If the patient is switching from Depo-Provera to Norplant, Norplant can be inserted 12 weeks after the last injection. No barrier method of protection is needed with this switch.
- If the patient desires to switch to oral contraceptives, she should start the oral contraceptives 12 weeks after the last injection.

K. Managing Heavy Bleeding While on Depo-Provera

- Because Depo-Provera can thin the endometrial lining making it unstable, at times the patient may experience heavy bleeding. Control of bleeding under these circumstances may be obtained by the following:
 - ◆ Make sure the patient is not pregnant
 - ◆ NSAIA may be tried
 - ◆ Add a low dose monophasic combined oral contraceptive for 2-3 cycles, or
 - ◆ Add 20 mcg ethinyl estradiol daily for 2-3 months; if necessary physiologic estrogen replacement therapy may be continued indefinitely
 - ◆ Add premarin 1.25 mg daily for 2-3 months.
 - ◆ If you have added estrogen, advise a back-up method of contraception as ovulation can occur.

References

- Bigrigg A, Evans M, Gbolade B, Newton J, Pollard L, Szarewski A, Thomas C, and Walling M. Review Article: Depo Provera. Position paper on clinical use, effectiveness and side effects. *British J of Family Planning* 1999; 25:69-76.
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- Davis, AJ. *Common Contraceptive Questions and Dilemmas, Syllabus, Gynecology for the Non-Gynecologist*, Boston, 1998.