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Depo-Provera and Weight Gain

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For many years women of reproductive age had few recourses when it came to preventing unwanted pregnancy. Although various methods of contraception existed, women were often faced with a choice between convenience and efficacy. In recent years, however, the hormonal contraceptive Depo-Provera® (Pharmacia & Upjohn Company, Kalamazoo, MI) has appeared to solve these problems, suggesting itself as a nearly "ideal" contraceptive. An "ideal" contraceptive is considered to be a method that encourages a high degree of compliance, is discreet, is reversible, has minimal side effects, and is nearly 100% effective (1). Depo-Provera® does all of these, yet its use is by no means the widespread phenomenon one would expect. This could be due in part to perceived or actual side effects that discourage women from choosing Depo-Provera®. This paper considers the question of weight gain as a side effect of Depo-Provera® use for which there is variable and often contradictory information.

Depo-Provera® Contraceptive Injection (depot medroxyprogesterone acetate or DMPA) contains a synthetic hormone derivative of progesterone as its active ingredient. Approved by the Food and Drug Administration (FDA) for use as a contraceptive in the United States in 1992, DMPA primarily functions by inhibiting the secretion of gonadotropins. This, in turn, prevents follicular maturation, suppressing ovulation and generating the desired contraceptive effect. The 150mg/ml DMPA injection is administered intramuscularly once every 12-13 weeks (11). However, like any pharmaceutical intervention side effects must be considered and can be contraindications for use. Product information suggests that 60% of patients experience a weight gain anywhere from 4-6 pounds in the first six months of use (10). Early studies looking at DMPA support this observation. Landmark studies done on clinic populations during the 1970s show an increase in the mean body weight of the patients over time (8). This weight increase appears to be maintained as long as the woman is on DMPA, although the amount of change during each year decreases with prolonged duration of therapy. One suggested reason may be the glucocorticoid-like activity of DMPA (9). It should also be noted that the initial weight gain is thought to be due, primarily, to an increase in water retention, and is reversed within a few months once therapy is discontinued (12).

Patient beliefs regarding the side effects of DMPA have been looked at in an attempt to see how people are choosing their contraceptives. It has been shown that patients choosing other methods of hormonal birth control rate DMPA as less satisfactory in both convenience and efficacy. Additionally, patients rated DMPA as having the most side effects, of which weight gain was a major concern. Physicians are often hesitant to recommend DMPA because of these beliefs and because of its known (or assumed) effect on weight (4). This is especially true in the United States where the generally accepted standard of beauty requires women to be at or under an ideal weight. A gain of 4-6 pounds for an adolescent in the United States may be more psychologically damaging than a similar weight gain would be for an adolescent or young adult in another country where the accepted standard of beauty allows for a higher weight per given height and body structure. In studies done in Egypt, a small weight gain was noted with continued injections. However, this was not seen as a negative. Rather, it was welcomed by the participants and was clearly not implicated in a decision to discontinue use (7). Research done on patients in the United States indicates that weight gain is a major complaint of women on DMPA, and is an important factor in discontinuation of this method (7). Sangi-Haghpeykar et al noted that weight gain was the most common side effect reported by their patients. Over the 9 month study period anywhere from 38-46% of participants complained of weight gain, although the amount

gained was not noted. Of the patients that stopped using DMPA weight gain was one of the most common complaints noted and was frequently listed as a reason for discontinuation.

Despite this evidence and the anecdotal reports of DMPA users, recent data looking at weight changes with different hormonal contraceptives does not indicate significant amounts of weight gain in users of DMPA (3). In a study by Mainwaring et al (3), metabolic parameters (cholesterol level, triglycerides, low density lipoprotein (LDL), high density lipoprotein (HDL)) were observed as well as body weights. No significant changes in pre- and post-therapy weights for DMPA users were detected after one year of therapy. In general, there was a gain of 1-3 pounds above the mean starting weight and one woman gained over 40 pounds. Moore et al(4) also looked at weight gain among users of different types of hormonal contraception. The mean weight was slightly increased for the DMPA users (.13 pounds) over a twelve month period, however this is not considered significantly different from zero. Thus, here again the statistical data clearly counters the data released by the Pharmacia & Upjohn Company, and is contradictory to previous data as well. Looking at the demographic data in the Mainwaring and Moore studies provides no explanation for this contradiction. The age ranges for the majority of studies was similar ranging from adolescents to adult women. However, it was noted in one study that users of DMPA tend to be younger than users of other oral contraceptives. This may have some affect on weight gain (4). One study, cited by Bromham indicated that weight gain in that patient population could be attributed to the age change during the course of the study (1). It should be noted that many users of DMPA in developed countries like the United States are younger in age than users in developing countries (1). This may be a result of the tolerance of earlier sexual activity in developed nations. This age difference between United States and foreign DMPA users may, in part account for the lack of change in weight. Older users clearly have different metabolisms and often have different activity levels than younger women and adolescents. Thus, even a year of aging at 30 may produce a greater weight change, simply in response to the normal aging process. Younger women, whose metabolisms are still fairly high, may not experience this weight gain due to their normal compensatory mechanisms provided by their metabolism. This may also explain the difference in outcome in prior research vs. current research. The landmark studies conducted nearly 30 years ago looked at women with a mean age (30 years) above that of the more recently studied adolescents and young women (mean ages 22-26). These age differences may be confounding variables inherent in the research but has not been carefully looked at.

In summary, DMPA or Depo-Provera® is a birth control method that must be considered carefully, both by the patient choosing to use it and by the physician prescribing its use. While product information is careful to warn users of the potential for significant weight gain, empirical evidence both supports and refutes this claim. For some users the convenience and efficacy, previously unavailable, outweighs their potential concern regarding weight gain. However, for others, especially adult or unmarried women in the United States, a weight gain of only a few pounds can not be tolerated. Research which investigates weight changes among different age groups, as well as research comparing DMPA users to non-hormonal contraceptive users is lacking. Furthermore, research that examines the cause of the noted weight gains is non-existent, and should be considered as a possible area of increased investigation.

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