

## PREVENTION OF INFERTILITY SOURCE DOCUMENT

### **ABNORMAL BODY WEIGHT:** **A PREVENTABLE CAUSE OF INFERTILITY**

On a recent CBS Evening News Report, the claim was made that 50% of Americans are overweight and that more than 30% of Americans are obese. The “girth” of Americans is increasing at a rate faster than any other people of the world. Fast foods along with changing cooking and eating habits are the purported causes of growing American obesity.

Obesity immediately brings to mind associations with hypertension, diabetes and heart disease. Yet, most people are surprised to learn that there is an association between obesity and infertility. Adam Smith describes in *The Wealth of Nations* the impact of body weight on reproduction. He writes that the poor women of Edinburgh (slender due to inadequate diet) have difficulty conceiving, while the rich women (those with an adequate diet) have no problem conceiving. Epidemiological data confirm that obesity accounts for 6% of primary infertility, and even more surprising, that low body weight in women accounts for 6% of primary infertility. Thus, 12% of primary infertility results from deviations in body weight from established norms, and that this infertility can be corrected by restoring body weight to within normal established limits.

More than 70% of women who are infertile as the result of body weight disorders will conceive spontaneously if their weight disorder is corrected through a weight-gaining or weight-reduction diet as appropriate. Yet, body weight is often considered last in an infertility evaluation. It may be ignored entirely until other diagnostic studies and therapeutic interventions have proven normal or futile. In my opinion, the body weight of both partners of the infertile couple should be considered first when there is an obvious slender or obese body habitus *in either partner*. Also, awareness of the importance of body weight on reproduction enables couples to maintain appropriate body weight or to correct a body weight disorder before subjecting themselves to expensive, time consuming infertility evaluation and treatment.

### **Mechanisms For Alteration Of Reproductive Function**

What is the relationship between body weight and infertility? Sex steroid hormones—testosterone (the principal male hormone) and estradiol (the principal female hormone)—are lipid soluble, i.e.; they dissolve in fat but not in water. Thus, these hormones accumulate in body fat. Once body fat stores are saturated with sex steroid hormones, they reach equilibrium with blood. In addition to the stored source of sex steroid hormones in body fat, the gonads secrete testosterone and estradiol to maintain the levels necessary to sustain reproductive function.

In addition to the storage capacity of body fat for sex steroid hormones, adipose cells (fat cells) convert the weak male hormone, androstenedione, to the weak female hormone, estrone. Estrone, though not as potent as estradiol, has metabolic effects on the hypothalamic-pituitary axis of the brain (the area of the brain that regulates testicular and ovarian function) to alter reproductive function. These complex interactions have the net effect of impairing reproductive function. These effects of body weight on female reproductive function are well established.

However, the effects of body weight on male reproductive function are not well studied and are more speculative.

There are differential metabolic pathways for estradiol metabolism in women depending on body weight. Slender women metabolize estradiol to 2-hydroxyestrone—an antiestrogen; obese women metabolize estradiol to estriol—a weak estrogen. The rate of metabolic change seems to correlate with the percent of body fat of total body mass. Thus, slender women progressively “turn down” the reproductive cycle until it is “turned off” when the condition of anorexia nervosa (defined as less than 85% of predicted ideal body weight for height) is reached. On the other hand, obese women progressively increase their alternate estrogens—estrone and estriol—until ovulation ceases and they become infertile. It is ironic that both thin and obese women develop irregular reproductive cycles, but by entirely different mechanisms. Thin women are estrogen deficient whereas obese women have an excess of estrogen but do not cycle on a regular basis.

It is well established that body fat affects the onset of puberty in girls. Most of us have observed early breast development in “chubby girls” and delayed breast development in thin girls. Girls who participate in strenuous training programs such as gymnastics or ballet have delayed puberty. Their secondary sexual development (breasts, pubic hair, menstruation, ovulation) does not occur until they reduce or stop their training program and increase their body fat.

There are reports of earlier puberty in girls during the past decade. This may reflect the relationship between body fat, a fast-food diet, and secondary sexual development. If we relate the earlier onset of puberty to the early accumulation of body fat, it is likely that sufficient estradiol is being sequestered in body fat to initiate secondary sexual development. With progressive accumulation of body fat that approaches obesity (as defined as greater than 120% of predicted ideal body weight for height) in adolescent girls, reproductive function may begin as a normal physiologic event and progress to impairment of reproductive function within a few years. Not only should adults be aware of this relationship between body weight and reproductive function, but parents should be aware of the relationship as well. Parents can counsel their adolescent children about the impact of body fat on the secondary sexual development and reproductive function of their adolescent children.

Despite the number of publications, both scientific publications and lay publications in the media, there is lack of knowledge about the relationship between body weight and infertility. This paper is an effort to further educate about this relationship so those couples contemplating pregnancy can assess their body weight as it pertains to their potential to conceive a pregnancy. This is an opportunity for infertile couples to understand the impact of body weight on their reproductive capacity and take steps, without expert advice, to improve their reproductive capacity.

### **Recognizing reproductive changes**

The *sine qua none* of normal reproductive function in women is regular, predictable menstrual cycles. Most women will cycle at 26-32 day intervals on a predictable basis. In males, the *sine qua none* of normal reproductive function is morning erections. The latter equates with normal

testosterone secretion, but does not correlate with a normal sperm count. Thus, men must have a semen analysis to establish reproductive potential.

The first sign in women of altered reproductive function is variation from an established regular, predictable menstrual cycle. Moreover, ovulating women will experience abundant, clear mucous secretions from the vagina at mid-cycle as well as breast fullness, breast tenderness and abdominal bloating during the week prior to menstruation. Abundant cervical mucous (perceived as vaginal mucous) correlates with appropriate mid-reproductive cycle estradiol secretion by the ovaries, while the latter signs of breast fullness, breast tenderness and abdominal bloating correlate with progesterone secretion following ovulation. The absence of these signs suggests altered ovulatory function.

Obese women experience first, a change in their reproductive cycles. Their cycles become irregular, unpredictable and often heavy and prolonged. Heavy, prolonged cycles correlate with increased estrogen production in the forms of estrone and estriol. In addition, obese women will often notice the onset of dark (terminal) hair on the lower abdomen, face and between the breasts. This terminal hair results from the increased ovarian production of androstenedione that occurs with obesity. Although androstenedione is a weak male hormone, over time it will stimulate excessive body hair growth.

Slender women experience different signs and symptoms from obese women. The initial sign of altered reproductive cycles is similar to that of obese women. However, as estrogen production decreases, slender women experience decreasing vaginal mucous secretions as well as decreased breast size. Eventually, slender women experience vaginal dryness and loss of sex drive.

Again, women who experience these signs and symptoms associated with changes in body weight can make the correlation, evaluate and treat themselves. If they seek professional medical attention, their physician(s) should support their self-evaluation and encourage them to correct their weight problem.

### **Treatment of weight-related reproductive disorders**

Obese women are more apt to acknowledge the impact of obesity on reproductive function than are slender women. However, the challenge of weight loss is just as daunting as is the challenge of weight gain for slender women. Most obese people (men and women) have tried diets, exercise programs and other methods to lose weight, but have not been successful. When a physician recommends a weight reduction program for obese people trying to conceive, the patient (couple) often views this recommendation as another wasted effort

The approach that a physician takes to weight reduction shapes the outcome. Obese women need education and counseling. Moreover, they need encouragement and understanding with praise for accomplishments for weight reduction.

Because many obese women have an excess of androstenedione, the administration of oral contraceptives will suppress the pituitary signal (leutinizing hormone) that stimulates the ovaries to overproduce androstenedione. Obese, infertile women find it a paradox that birth control pills facilitate pregnancy!

In addition to oral contraceptives, the traditional methods of weight loss—diet and exercise—are essential elements of the treatment program. It must be emphasized to obese individuals that weight loss does not occur immediately, but must be measured over time. It is realistic to anticipate weight loss at the rate of one pound per week. Thus, if the objective is a 20-pound weight loss, then a minimum of 20 weeks is required to achieve this objective. Unrealistic expectations lead to abandonment of the weight loss program. Obese individuals should set their goal to reach a body weight that is 110% of predicted ideal body weight.

Slender women are more challenging than obese women to accept the idea that low body weight contributes to infertility. Many slender women work at being slender. They diet strenuously, exercise vigorously and work to fit into a small size dress. It is hard to convince them that their “healthful” lifestyle contributes to their infertility.

The key to success with slender women is convincing them that low body weight is associated with infertility. Once this can be achieved, the rest of the therapeutic program comes easily. Slender women should be encouraged to increase their body weight to 100% of predicted ideal body weight for their height. They should gain weight at the rate of one-half pound per week. Since slender women work hard to maintain their svelte body habitus, it is easy for them to gain weight once they buy-in to the program. Weight gain should be slow and one expects that six months will be required to restore normal reproductive function and pregnancy.

### **Summary**

Body fat plays a critical role in human reproduction. Both excess and deficiency of body fat lead to reproductive failure. Body weight disorders is one of the first potential causes of reproductive failure in both men and women. This is a problem that can be corrected by the affected individual and the infertile couple.

Twelve percent or more of infertile couples have deviations from their ideal body weight as the cause of their infertility. If a woman’s body weight is less than 95% of predicted ideal body weight or greater than 120% of predicted ideal body weight, then appropriate weight gain or weight loss should be the primary therapeutic recommendation. These men and women need patience and understanding as they cope with the issue of body weight and its impact on their reproductive function.

Respectfully submitted to the Prevention of Infertility Committee by:  
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## **References**

1. Green BB, Weiss NB, Daling JR: Risk of ovulatory infertility in relation to body weight. *Fertil Steril* 50:721, 1988.
2. Bates GW, Bates SR, Whitworth NS: Reproductive failure in women who practice weight control. *Fertil Steril* 37:373. 1982
3. Bates GW, Whitworth NS: Effect of body weight reduction on plasma androgens in obese, infertile women. *Fertil Steril* 38:406, 1982.
4. Pigny P, Cortet-Rudelli C, Decanter C, Deroubaix D, Soudan B, et al: Serum levels of inhibins are differentially altered in patients with polycystic ovary syndrome: effects of being overweight and relevance to hyperandrogenism. *Fertil Steril* 73:972,2000.
5. Bates GW: Body Weight and Reproduction. In Seibel MM, *Infertility: A Comprehensive Text*. Appleton-Century-Crofts. New York, 1996.
6. Frisch RE, McArthur J: Menstrual cycles: fatness as a determinate of minimum weight for height for their maintenance and onset. *Science* 185:949, 1974.
7. Warren MP: The effects of exercise on pubertal progression and reproductive function in girls. *J Clin Endocrinol Metab* 51:1150,1980.