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OBESITY IN PREGNANCY AND BEYOND

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Introduction

One of the least rewarding experiences in clinical medicine is treating obesity. Because from 40 to 60 percent of American adults over 30 years old are more than 20 percent over weight, the unrewarding fight against obesity is all too common. Not only with our patients, but with ourselves. Unfortunately, for over 100 years the incidence of obesity has been increasing in the United States, a reflection of an increasingly sedentary life in an affluent society. The death rate from diabetes mellitus, for example, is approximately four times higher among obese diabetics than among those who control their weight. Also higher among individuals is the incidence of gall bladder disease, cardiovascular disease, renal disease, and cirrhosis of the liver. The death rate from appendicitis is double, presumably from anesthetic and surgical complications. Even the rate of accidents is higher, perhaps because fat people are awkward or because their view of the ground or floor is obstructed. When the personal and social problems encountered by obese persons are also considered, it is no wonder that a physician without a weight problem cannot comprehend why fat individuals remain overweight.

As a basis for a more understanding approach to obesity we are going to review the physiology of adipose tissue, discuss differences between normal and obese people and commend on treatment.

Definition Of Obesity

There is a difference between obesity and overweight. Obesity is an excess of body fat. Overweight is a body weight in excess of some standard or ideal weight. The ideal weight for any adult is believed to correspond to his or her ideal weight from age 20 to 30. The following formulas give ideal weight in pounds:

Women:[100 + 4 X (height in inches - 60)]

Men: [120 + 4 X (height in inches – 60)]

At a weight close to ideal weight, individuals may be overweight, but not over fat. This is especially true of individuals engaged in regular exercise. An estimate of body fat, therefore, rather than a measurement of height and weight, is more significant. The best method to determine body fat is to determine the density of the body by underwater measurement. However, since this technique is impractical a body mass index nomogram is the best way to do things in a clinical setting. The body mass index is calculated as the ratio of weight divided by the body surface squared (in metric units).

A body mass index of about 30 is roughly equivalent to 30 percent excess body weight, the point at which excess mortality begins. Above 40%, the risk from obesity itself, is comparable to that associated with major health problems such as hypertension and heavy smoking.

A person is obese when the amount of adipose tissue is sufficiently high (20 percent or more over ideal weight) to detrimentally alter biochemical and physiologic functions and to shorten life expectancy. Obesity is associated with four major risk factors for arteriosclerosis: hypertension, diabetes, hypercholesterolemia, and hypertriglyceridemia. Overweight individuals have a higher prevalence of hypertension at every age, and the risk of developing hypertension is related to the amount of weight gain after age 25. The two in combination (hypertension and obesity) increase the risk of heart disease, cerebral vascular disease and death.

The basal metabolic rate decreases with age. After age 18, the resting metabolic rate declined about 2 percent every decade. A 30 year old individual will inevitably gain weight if there is no change in caloric intake or exercise level over the years. The middle age spread is both a biological and a psychosociological phenomenon. It is therefore, important for both our patients and ourselves to understand adipose tissue and the problem of obesity.

PHYSIOLOGY OF ADIPOSE TISSUE

Functions of Adipose Tissue

1. Adipose tissue is a storehouse of energy.
2. Fat serves as a cushion from trauma.
3. Adipose tissue plays a roll in the regulation of body heat.

When fat is absorbed from the gastrointestinal track, it goes through the liver where a new lipoprotein is produced and released in the circulation. This lipoprotein is transferred to the adipose tissue where it is broken down by lipase into fatty acids, which then are stored into the fat cells as triglycerides.

Glucose Function

1. Glucose supplies carbon atoms in the form of acetyl coenzyme A.
2. Glucose provides hydrogen for reductive steps.
3. Glucose is the main source of glycerophosphate. The presence of glycerophosphate is a rate-limiting factor in lipogenesis and of course, this process depends on the presence of glucose.

The chief metabolic products produced from fat are the circulating free fatty acids. Free fatty acid release from adipose tissue is stimulated by physical exercise, fasting, exposure to cold, nervous tension and anxiety. Omental, mesenteric, and subcutaneous fat are more labile and easily mobilized than fat from other sources. Lipase activity is inhibited by insulin, which appears to be alone as the maior physiologic antagonist to the array of stimulating agents. The presence of glucose and insulin promotes production of glycerophosphate which then promotes triglyceride deposition in the fat

cells. To put the above in a simple way, when a person eats, glucose is available, insulin is secreted, and fat la stored. In starvation, the glucose level falls, insulin secretion decreases, and tat is mobilized. When single large meals are consumed, the body learns to convert carbohydrate to tat very quickly There has been a good correlation between fewer meals and greater tendency toward obesity

CLINICAL OBESITY

Obesity and the Brain

The hypothalamic location of the appetite center was established in 1940 by the demonstration that bilateral lesions of the ventromedial nucleus produce experimental obesity in rats. There may be two kinds of obesity: Obesity stemming from a CNS regulatory defect, or obesity due to a metabolic problem occurring despite a normal central mechanism for appetite.

Psychological Factors

Obese and lean people respond differently to their environments. Obese people appear to regulate their desire for food through external signals. Lean people, on the other hand, regulate their intake by endogenous signals of hunger and satiety. Fear does not inhibit GI activity and dull the appetite in obese persons as it does in others. Fat people eat because it is meal time, and food looks, smells, and tastes good. They also eat because other people are eating, but not necessarily because they themselves are hungry.

Obese people are also less physically active than are people of normal weight. The obese person will drive a car around the block repeatedly until a parking space is available, rather than walk a few blocks. There may be two classes of obesity: One class may include those who clearly eat too much and the other class would be composed of individuals who eat relatively normal diets, but who are extremely inactive.

Fat Cells

The development of obesity is determined by many factors. The number of the preadipocytes which is determined prenatally is important. Normal fetuses are born with approximately five billion cells from adipose tissue which represents 16 percent of the total number of cells found in the adult (30 billion cells). During postnatal development and In the first ten years of life, the total number of mature adipocytes progressively increases. This increase parallels the overall growth of the human body. During puberty there is a higher increase of adipocytes to the point that by the end of puberty the number is similar to the adult population. It is suspected that when the existing adipocytes reach a critical size a local factor stimulates preadipocytes that transform themselves into adipocytes and thus we have hyperplasia as a follow-up to hypertrophy. Genetic factors also play a roll. Studies performed on monozygotic and dizygotic twins helped us estimate the heritability for body fat to be 0.88. High heritability of adipose tissue development is well documented in animals. It is also true

that by the age of 17, children of two obese parents are three times as fat as the children of two lean parents. Of course, in these studies it is not possible to separate acquired traits from inherited traits. Finally, maternal diet affects fetal development of adipose tissue. Nutritional deprivation in the third trimester can lead to small for dates infants and decrease the incidence of obesity. In contrast, deprivation during the early pregnancy, first and second trimester, even in the presence of continued deprivation during the third trimester leads to increased incidence of obesity in postnatal life. This is suspected to be the result of intrauterine life adaptation of the hypothalamus and other endocrine systems. Overexposure to energy and increased growth in the third trimester leads to obesity in postnatal life also.

The effect of nutritional status on postnatal adipocyte development was recently reviewed by Lemonnier. Over consumption of energy primarily leads to hypertrophy and subsequently, to hyperplasia with proliferation of adipocytes. It is interesting to note that animal fat causes both hypertrophy and hyperplasia while unsaturated fat diets increase only the adipose cell size without hyperplasia.

Petite et al in the Journal of Diabetes Care, Volume 16, Supplement 1/ January 1993 reviewed diabetes and obesity in the offspring of Pima Indian women with diabetes during pregnancy. They found that the offspring of women who had diabetes during pregnancy on the average, were more obese and had higher glucose concentrations and more diabetes than the offspring of women who developed diabetes after pregnancy or who remain nondiabetic. They concluded that diabetic pregnancy, in addition to its effects on the newborn, has effects on the subsequent growth and glucose metabolism of the offspring. These effects are in addition to genetically determined traits.

Endocrine Changes

The most important endocrine change in obesity is elevation of the basal blood insulin level. Increases in body fat change the body's secretion and sensitivity to insulin. The key factors which affect insulin resistance are the amount of fat tissue in the body, the caloric intake per day, the amount of carbohydrates in the diet, and the amount of daily exercise. The mechanism for the increased resistance to insulin observed with increasing weight may be down-regulation of insulin receptors brought about by the increase in insulin secretion.

Other endocrine changes associated with obesity include decreased growth hormone secretion, and increased cortisol production and metabolic clearance rates (thus, plasma and urinary cortisol are relatively normal). Fasting levels of growth hormone are decreased as well as the response to insulin, arginine, starvation and sleep. There is evidence of decreased pancreatic alpha cell function in obese nondiabetic people. Glucagon secreted by the alpha cells acutely raises blood glucose levels by stimulating hepatic glycogenolysis and the production of new glucose from amino acids in the liver. Glucagon also activates lipolysis in the fat cell and stimulates insulin secretion. The basal levels of glucagon are equal in obese and non obese patients, but the glucagon response to alanine is reduced by 50 percent in the obese group.

Anatomic Obesity

There are two types of anatomic obesity: gynoid and android. Gynoid obesity refers to fat distribution in the lower body (femoral and gluteal regions), while android obesity refers to upper body distribution. Gynoid fat is mainly stored fat and more difficult to mobilize than android which is primarily located in the abdominal wall and visceral-mesenteric locations. The waist to hip ratio is a means of estimating the degree of upper to lower body obesity. The ratio is obtained by measuring the body circumference at the level of the umbilicus and the anterior iliac crests. If the ratio is greater than 1.2, we have android obesity. A ratio between 0.6 and 1.2 is normal and a ratio less than 0.6, is indicative of gynoid obesity.

MATERNAL AND FETAL/ NEONATAL RISKS FROM OBESITY

Defining obesity in pregnancy is a difficult task. Most of the studies in the past that have looked upon the effect of obesity on pregnancy outcomes did not follow a consistent definition of obesity. This has created a number of conflicting reports or plainly a number of invalid reports. Unless obesity predated the pregnancy, increasing weight alone is not sufficient to define a pregnant patient as obese given the fact that a significant number of women gain substantial amounts of weight secondary to fluid retention.

Aside from the difficulties in defining obesity and by accepting these limitations, Is obesity really a risk factor for the pregnant woman and her fetus? Almost all of the studies that have evaluated the effect of obesity on the health of the mother have found that obese pregnant women are at increased risk to develop gestational diabetes, hypertension (chronic and preeclampsia), twins, dysfunctional labor patterns, anesthesia and operative risks, post-partum hemorrhage, thrombophlebitis, and wound infection/dehiscence. In a recent review over the international literature from 1960 to 1982 performed by Suzanne Ruge, 143 studies were identified and approximately 26 of them fulfilled the criteria of the study and were analyzed. A total of 10,440 cases were part of the analysis and most of the reported subjects were only moderately obese. Thirty-seven complications were stated in one or more publications as being significantly more prevalent among obese women compared with lean controls. However, as data were often scarce or highly conflicting, it is concluded that an increased risk is only sufficiently documented with regards to a minority of these complications. They are: pre-eclampsia as well as each separate element of this disorder, diabetes mellitus, varicose veins, and the need for cesarean section. The significantly increased birth weight of infants did not induce a corresponding increase of labor complications.

Gross, et al. found the incidence of Class A diabetes to be 6.5% in their obese patients compared with 0.8% of non-obese patients. An additional problem in obese women is the occurrence of both chronic hypertension and the development of superimposed preeclampsia or eclampsia. Seven percent of obese women begin the pregnancy with chronic hypertension, whereas leaner patients had a lower incidence at 1.5% The most predominant problem associated with obese pregnancies is the development of fetal macrosomia and its potential effects on the course of labor and delivery. Approximately 15 to 33% of the term infants of obese mothers weighed greater than 4000 grams, compared with 4 to 5% of the leaner women's infants. This increased incidence of macrosomia in obese women happens regardless of the amount of weight gained during the pregnancy; even obese women who have gained less than 6 kilograms (14 pounds) have an increased incidence of macrosomia in their offspring. This excessive fetal growth in part may be the result of coexisting

carbohydrate intolerance, but the biggest part is not explained by the presence of diabetes but only by the presence of maternal obesity.

It has been consistently observed that the infants of obese mothers weigh more at term birth than the infant of a lean mother. In addition, the incidence of low birth weight, preterm and IUGR infants is reduced. In general macrosomic infants are at increased risk for birth trauma associated with difficult deliveries. These include injury to the cranium, peripheral nerves, spine, extremity bones and clavicle, and hematomas of the liver or adrenal gland. The somatic growth of the fetus of the obese mother is characterized by enhanced adipose tissue deposition. Metabolically these fetuses also demonstrate high cord blood triglyceride levels. As triglycerides do not cross the placenta, fetal hepatic and/or adipose tissue esterified fat synthesis must be augmented in the fetus of an obese woman. Fetuses of obese women experience hypoglycemia but not to the degree of macrosomic babies of diabetic mothers. Usually babies of obese mothers are asymptomatic during a hypoglycemic episodes.

Robert Rutner, et al in two recent publications have demonstrated that in morbidly obese women (more than 160 % ideal body weight) there was no correlation between maternal weight gain and pregnancy complications. The data were analyzed for the development of gestational diabetes, pregnancy induced hypertension, pre-eclampsia, preterm labor, premature rupture of membranes, incompetent cervix and intrauterine growth retardation. When they examined the same patients for neonatal outcomes they found that patients who gained less than ten pounds did not have any different outcomes in terms of fetal growth in comparison to patients who gain more than ten pounds. This study reconfirmed the previous impression that obese women get normal size or even macrosomic fetuses regardless of weight gain. That points to the fact that these women supply their fetuses with alternate metabolic fuels from their fatty stores.

Risks associated with anesthesia complications

Anesthesia can pose additional risks to obese women in relation to non obese pregnant women. In a recent report of anesthesia related maternal mortality in Michigan, obesity was a risk factor in 80 percent of patients who died. Some other studies have also shown similar results. Some of the problems encountered during anesthesia in obese patients can be overcome by good preparation of the patient, and effective management and cooperation on the part of obstetrician and anesthesiologist can minimize other problems; but successful anesthesia care is based on an understanding of the changes underlying pregnancy and obesity and their interaction. Anesthesiologists dedicated to obstetrical anesthesia may be most suitable to minimize the risk to an obese patient during pregnancy.

Peripartum cardiomyopathy

It is believed that peripartum heart failure (idiopathic cardiomyopathy) is more prevalent in obese women. However, it is unclear whether it is obesity per se as a only factor or the cardiovascular implications of hypertension and chronic cardiac disease that afflicts obese women in addition to the increasing demands of the pregnancy. Cunningham et al studied the outcomes of 28 women who developed peripartum heart failure out of a group of 106,000 women. In 21 of these 28 women, heart failure was attributed to chronic underlying disease (chronic hypertension in 14, mitral stenosis in

four, and morbid obesity in one) or viral myocarditis. Importantly, these women also had multiple compounding cardiovascular factors (preeclampsia, cesarean section, anemia, and infection) which when superimposed on those of pregnancy, acted in concert to cause heart failure. In seven women, the cause for cardiomegaly and global hypokinesis was not found, and peripartum cardiomyopathy was diagnosed. It is then evident that obesity alone is not a significant factor for peripartum cardiomyopathy but certainly obesity with its concomitant medical complications may be involved in half of the patients who suffer this condition.

Maternal Fatness And Viability Of Preterm infants

A. Lucas et al have examined the outcomes of fetuses of obese mothers with birth weight less than 1850 grams. In 771 mother-infant pairs maternal age, complications of pregnancy, mode of delivery, parity, social class and the baby's sex and gestation were analyzed by a logistic regression model for associations with infant mortality (but deaths from severe congenital abnormalities in those occurring during the first 48 hours after birth were excluded). In a subgroup of 284 mother-infant pairs, all infant deaths except those from severe congenital abnormalities were analyzed in association with infant's birth weight and gestation and the mother's height and weight; this second analysis included another 24 infants who had died within 48 hours after birth. In the first analysis mortality overall was 7% (55/771), rising from 4% in the mothers with normal weight to 15 % in mothers with moderate and severe obesity. After adjusting for major demographic and antenatal factors, including serious complications of pregnancy, maternal fatness was second in importance only to length of gestation in predicting death of infants born preterm. In the second analysis mortality overall was 15% (44/284), rising from 9% in thin mothers to 47% in mothers with significant obesity. In both analyses, the relative risk of death by 18 months post-term was nearly four times greater in infants born to obese mothers than in those born to thin mothers. In addition, maternal fatness was associated with reduced birth weight, whereas it is associated with macrosomia in term infants. This data differ fundamentally from those reported in full-term babies of obese mothers. It is speculated that the altered metabolic milieu in obesity may reduce the ability of the fetus to adapt to extra uterine life if it is born prematurely.

Pregnancy After Gastric bypass For Morbid Obesity

D. Richards et al reported recently on 57 pregnancies from mothers who underwent gastric bypass prior to the pregnancy. These outcomes were compared to a group of controlled pregnancies occurring in morbidly obese women before their bypass surgery. There was a significantly lower incidence of hypertension and large for gestational age infants in the postoperative pregnancies. There was no significant difference in a number of other pregnancy complications studied. These complications include gestation diabetes, delivery at less than 37 weeks, cesarean section, peripartum blood transfusion, peripartum intravenous antibiotics for fever, thromboembolic disease requiring Heparin, small for gestational age neonates, perinatal death and newborn hospitalization for more than seven days. Fetal macrosomia was 9% in the postoperative group and 21% in the control group. Likewise, average birth weight in the postoperative group was 3,200 grams and in the control group was 3,600 grams.

Maternal Ketosis And its Effects On The Fetus

Pregnancy is associated with accelerated starvation ketosis. This phenomenon is evident after brief periods of fasting and represents an acceleration of the normal response to caloric deprivation. Maternal ketosis is readily transmitted to the fetus where ketone bodies are used as a source of fuel and as a substrate for lipid synthesis. In spite of these potentially useful functions, it has long been recognized that clinical conditions that accentuate maternal ketosis (diabetes, malnutrition) are associated with a less favorable fetal outcome. Are ketones really harmful to the fetus? The fuel fluxes that occur during pregnancy are a characteristic of a state of accelerated starvation, where hyperketonemia, hypoglycemia and occur more rapidly than normal. These metabolic changes are readily transmitted across the placenta. The fetus can utilize ketones as a source of energy and, therefore, seems to protect itself from the effects of maternal starvation. Ketones are also used by the fetus for lipid synthesis in the skin, 1ungs and brain, particularly for myelin synthesis. While there is considerable evidence that the fetus can readily utilize ketones, there are no direct experimental data showing that ketones per se are potentially toxic.

The clinical significance of ketosis during pregnancy has not been determined. However, considerable concern has been aroused following a study that suggested that maternal ketonuria of diabetes or other etiology has an adverse affect on the neuropsychological development of the infant. However, other studies, including an investigation of following intrauterine exposure to famine during World War II, are not entirely consistent with this concept. Furthermore, there is a notable lack of knowledge on the in vivo effects of hyperketonemia associated with such clinical conditions as malnutrition and diabetes, and the roll of factors other than hyperketonemia that coexist with these conditions (e.g. nutritional deficiencies).

Given the above concerns, it seems most prudent to avoid ketosis in pregnancy whenever this can be readily achieved. Since blood ketone levels in pregnancy triple by 18 hours of fasting, the avoidance of regular meals should be discouraged. Whereas diabetic uterus doses has a devastating effect in pregnancy, the clinical impact of more subtle elevations of ketones in the blood is unknown. Whether the reduction in ketosis following intensive insulin treatment has contributed to the improved outcome for the infant of the diabetic mother, cannot be answered at this time. Regardless of whether ketones per se have adverse effects, they, at least, appear to be clinical markers for an unfavorable environment for the fetus. In the absence of diabetes and in the presence of obesity mild ketosis secondary to inadequate energy intake is not believed to be a problem for the developing fetus.

MANAGEMENT OF OBESITY

Physician and patient relationship should be excellent. An agreement should be reached about the goals and the program implemented. It is realistic to loose 4 to 5 pounds in the first month and 20 to 30 pounds in four to five months.

Despite various fads and diet books, the best diet continues to be a limitation of calories between 900 and 1200 calories per day, the actual amount depending on what the individual patient will accept and pursue. The ideal diet should contain 40 to 45 percent carbohydrate, 20 percent protein and 35 to 40 percent fat.

Behavioral modification is quite important for many obese patients in order to achieve successful and long lasting results. Extreme regimens regardless of the type of restriction can be dangerous leading

to electrolyte disturbances as well as other metabolic derangements. Some of the liquid protein diets have been associated with deaths due to cardiac arrhythmias. The low calorie diets, which utilize protein and carbohydrates, supplemented with minerals and vitamins as the only source of nutrition should be used for only severe obesity and under medical supervision. These diets are still potentially dangerous. In general, these diets may provide a short term success but do not guarantee a long-term weight maintenance.

Anorectic drugs are also used for less short-term therapy to control hunger, especially at the beginning of a diet and at a plateau or relapse stage. Diuretics may also be important in the early stages of diet since many patients who loose fat, they do not necessarily loose weight because of the increased water retention. For psychological reasons and to promote the continuation of the regimen, diuretics may be quite helpful in some patients.

Surgical treatments and starvation should be reserved for patients who are morbidly obese. Both methods involve many potential problems and require close monitoring

A regular pattern of physical exercise reduces the risk of many medical complications and helps loose weight by promoting better health overall. Regular exercise also inhibits appetite and this is an added
advantage. Not infrequently, patients appear doomed to frustration and despair unless the physician can motivate them to increase physical activity. In all individuals, dieting is more effective when combined with physical exercise, this is especially true in chronically obese patients. In other words, the life style of an obese person must be changed to overcome the desire to be inactive (walk instead of riding). Only by significantly increasing caloric expenditure will the input-output equilibrium be disturbed.

The obese person feels trapped. Obesity leads to characteristic behavioral manifestations, including passive personality, frequent periods of depression, decreased self-respect, and a sense of being hopelessly overwhelmed by problems. But just as the endocrine and metabolic changes seem to be secondary to obesity, many of the psychosocial attributes surrounding obesity may also be secondary.

Motivation to change and emotional support during the change are important. Friends, relatives, physicians or self-help organizations can provide them. If the vicious circle of failed diets, resignation to fate, guilt and shame can be broken, a more effective happier person will emerge.