Preconception Nutrition: Conditions and Interventions

NUTD 238

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Premenstrual Syndrome (PMS)

 Characterized by life-disrupting physiological and psychological changes that begin in the luteal phase of the menstrual cycle and end with menstrual bleeding

Premenstrual Syndrome (PMS)

 The diagnosis of PMS is made when women exhibit
 1- 5 of the signs and symptoms in two consecutive luteal phases

TABLE 3.10 Common symptoms of PMS⁵²

| PHYSICAL | PSYCHOLOGICAL |
|--|---------------------------------------|
| Tender breasts | Angry outbursts |
| Abdominal bloating | Depression |
| Swelling | Irritability |
| Headache | Confusion |
| | Anxiety |
| | Social withdrawal |

• Premenstrual dysphoric disorder (PMDD) is a severe form of PMS

 ○ PMDD is diagnosed when ≥5 signs or symptoms of PMS occur during at least 2 consecutive menstrual cycles- 1 of the symptoms must be related to depression, anxiety, or mood swings



- Cause is unknown- might be related to an interaction between change in hormone levels after ovulation and neurotransmitters in the brain, mainly serotonin
 - Serotonin reuptake inhibitors (e.g., in antidepressants) effectively reduce PMS symptoms in some women

• To treat PMS:

- Decrease caffeine intake
- $\circ\,$ Exercise and stress reduction
- Consume Mg, Ca, or vitB6 supplements

• Caffeine

- Recommendation- reduce caffeine intake to decrease PMS symptoms
- $\circ~$ Research findings: $\uparrow~$ coffee intake $\uparrow~$ PMS symptoms severity

Exercise, stress reduction

- $\circ \ \uparrow daily \ PA \ and \ \downarrow daily \ stressors \ appear \ to \ diminish \ PMS \ symptoms \ in many \ women$
 - Regular PA tends to improve E level, mood, and feelings of well-being in women with PMS

• Mg

- Mg supplements of 200mg/d (safe- below UL) given during two cycles have been shown to decrease swelling, breast tenderness, and abdominal bloating symptoms of PMS
- $\circ~$ Not all studies show this +ve effect

Ca, Vit D, and PMS

Study findings:

- Ca supplements of 1200mg/d for 3 cycles were found to ↓ PMS symptoms of irritability, depression, anxiety, headaches, and cramps by 48%, vs. a reduction of 30% in placebo group
- Women with PMS were found to have lower intake and blood levels of vit D and Ca than women without the syndrome
 - The risk of developing PMS was 40% lower in women with avg vit D intakes of 17.7 mcg/ day vs. women consuming 2.8 mcg/d

Vit B6 and PMS

- Vit B6 is involved in the synthesis of neurotransmitters such as serotonin
- Serotonin receptor [] varies with changes in the estrogen and progesterone levels- people with PMS have lower blood [serotonin] leading to low mood, depression and sleep and appetite disturbances
- Some trials have found no effect of B6 on PMS symptoms, but others have identified benefits
 - → Dose range of 50- 100 mg/ day reduce the severity of premenstrual depressive symptoms in some women



• Obese men

 Low level of testosterone and sex hormone binding globulin (SHBG), low sperm count

Obese women

 $\circ~$ Highly irregular or an ovulatory cycles/ high levels of estrogen

Table 3.3 Biological bases of infertility in obese men and women^{17,22,23}

Men

- Low testosterone and sex hormone binding globulin levels
- Elevated leptin, follicle stimulating hormone (FSH), and estrogen levels
- Decreased sperm count, sperm motility; increased malformed sperm
- Oxidative stress, inflammation

 High estrogen, freetestosterone, and leptin levels

Women

- Reduced levels of sex hormone binding globulin
- Insulin resistance

 Oxidative stress, inflammation

Obesity and insulin resistance

- *Insulin resistance (IR)* frequently occurs along with obesity and contributes to adverse hormonal changes that affect fertility:
 - Insulin can bind to specific receptors on the ovary and stimulate testosterone production
 - Testosterone suppresses follicular growth, leading to ovulatory dysfunction

Obesity and chronic inflammation

• Low-grade inflammation

- Chronic inflammation: lasts wks, mos, or yrs; it is the first response of the body's immune system to infection or irritation. It triggers the release of biologically active substances that promote oxidation and other potentially harmful reactions in the body
- Can damage developing eggs and maturing sperm

Obesity and metabolic syndrome

Definition: Metabolic syndrome is not a specific disease but rather a cluster of abnormal metabolic and other health indicators. It is diagnosed when three of the following five conditions exist:

- Waist circumference >40" in men, >35" in women (These are an indicator of the presence of insulin resistance. Other population-based definitions of elevated waist circumference may also be used.)
- 2. Blood triglycerides $\geq 150 \text{ mg/dL}$
- 3. HDL-cholesterol <40 mg/dL in men and <50 mg/dL in women
- 4. Blood pressure of \geq 130/85 mm Hg
- 5. Fasting blood glucose $\geq 110 \text{ mg/dL}^{25}$

Prevalence: It is estimated that one in four U.S. adults has metabolic syndrome.²⁶

Major physiological aspects and consequences: The cluster of metabolic risk factors found in people with metabolic syndrome greatly increases the risk of development of cardiovascular disease and type 2 diabetes. Metabolic syndrome is also characterized by *chronic inflammation* that promotes oxidation reactions. Over time, chronic inflammation damages cells and body functions and can impair reproductive functions in both women and men.^{19,22}

- Therapy includes: lifestyle changesdietary modifications, wt reduction, & exercise
- Diets high in antioxidant-rich fruits, veges, whole-grains, fiber, and lowfat dairy products- ↓ inflammation, plasma TG and glucose, BW, and BP, ↑HDL-sC
- Risk factors: Obesity esp central obesity, IR

METABOLIC SYNDROME

What is Metabolic Syndrome?

Metabolic syndrome describes a common condition in which obesity, high blood pressure, high blood glucose (Piblood sugar), and an abnormal cholesterol profile (dyslipidemia) cluster together in one person. When these risk factors occur together, the chance of developing coronary heard disease, struke, and diabetes is much groater than when these risk factors develop independently. According to the American Heart Association, almost 25% of Americans are infected by metabolic syndrome.

Apple-shaped:

the abdomen.

Excess fat mostly around

Metabolic Syndrome Risk Factors

To be diagnosed with metabolic syndrome, patients need to have at least three of the following risk factors:

Obesity

Observing the defined as having hoe much body fat. A person is considered obsee when his /her weight is 20% or more above ideal weight. Observing promotes insulin resistance, an inability to respond normally to insulin. People with fat situated mainly around the stornach fadeomero are considered "apple-shaped". They have a higher risk of many of the serious conditions associated with metabolic syndrome. Ask your healthcare provider what your ideal weight should be.

> Metabolic Syndrome Risk Factor: Waist measurement greater than 35 inches (women) or 40 inches (men)

High Blood Glucose

Sugar (glucose) is what supplies the body with energy. Normally, this sugar (glucose) is rapidly (duared from the blood and sterred as energy. If sugar stays in the blood it causes an unballity building called high blood glucose. Edicose in the blood reaches all of the body is organic and systems, including the burt, arteries and verinx, kidneys, and nervcoss system. This constant "sugar-ratick" has the same affect as outing to much cauby and not brushing your teeth-it causes organ system docay or degeneration. People with high blood glucose are at trick for many diseases including hourit attack, which, Bindmess, and amputation. High blood glucose levels (or pre-diabetes) often leads to the development of type 2 dlucters.

> Metabolic Syndrome Risk Factor: Glucose of at least 110 mg/dL or greater

High Blood Pressure

Blood pressure is the force that helps the blood flow through the blood vessels. When the blood pressure in the arteries is too high, it is called high blood pressure. High blood pressure damages blood vessels. If blood vessels are subjected to high blood pressure for an extended period of time, they thicken, and become less flexible. This is called **arteriosclerosis**, and it can affect the arteries that surphy blood to the heart.

Blood pressure is measured using two numbers. The first number, called systolic pressure, is measured just after the heart contracts and the pressure is groatest. The second number is diastolic pressure. It is measured when the heart relaxes and the pressure is lowest.

Normal blood pressure is about 110/75 mmHg. High blood pressure alone causes no symptoms, but it does increase the risk of hourt attack, stroke, and kidney failure.

> Metabolic Syndrome Risk Factor: Blood pressure greater than 130/85 mmHg

Abnormal Cholesterol Profile (Dyslipidemia)

Cholesterol is a type of fat in your block. Cholesterol either cornes from the foodsyou eat or is mode by your inver. It is found in all of the body's cells. There are "good" and "had" types of cholesterol. Too much of the "bad" cholesterol (tinglycerides and LDL) and not enough "good" cholesterol UBU) can increase your risk of coronary heart disease. Triglycerides and HDL levels are important indicators of metabolic syndrome.

Triglycerides

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High triglyceride levels in the blood can help clog the arteries with fatty deposits called plaque (atherosclerosis), making it difficult for oxygen-rich blood to reach the heart. High triglyceride levels increase your risk of having a heart attack.

> Metabolic Syndrome Risk Factor. Triglyceride level greater than 150 mg/dL

HDL Cholesterol

HDL, choistered (the "good cholesterol") helps remove deposits from within the blood vessels and it stops the blood vessels from becoming blocked. The more HDL in your blood, the better it is for your heart. When HDL cholesterol levels are low, there is a greater risk of developing a heart attack or stroke.

Metabolic Syndrome Risk Factor: HDL cholesterol level less than 50 mg/dL (women) and less than 40 mg/dL (men Organs Affected by Untreated Metabolic Syndrome



- Balanced, healthy diets- provide all required nutrients in amounts recommended
- Address nutrient deficits in dietary plan
- For wt loss maintenance- wt should be lost slowly and accompanied by acceptable changes in diet, PA, and other lifestyle behaviors
- Set small, acceptable changes in diet and exercise that are sustainable

- Wt-loss surgery→ last resort for wt loss for obese individuals
- BMI> 40, or> 35 kg/m² if a serious medical condition related to obesity exists
- It generally reduces body wt to levels that qualify as overweight or somewhat obese
- In most cases → return to normal hormone levels, ↓ inflammation, and improved fertility

• Long term, benefits of fat loss related to the surgery include:

- Resolution of type 2 diabetes in 40% of individuals
- Improved glucose control
- Reduction of the risk of developing gestational diabetes and HTN during pregnancy

Surgery complications

- Increases risk of developing deficiencies including Fe, folate, Ca, and vitamins A, B12, and K
 - Risk of these deficiencies increases if chronic vomiting or malabsorption are present/ or when supplements are not taken
- If uncorrected, nutrient deficiencies can impair fetal growth and nutrient stores of the infant
 - Pregnancy is not recommended during the <u>1st year after</u> <u>bariatric surgery</u> when wt loss is most rapid

Hypothalamic Amenorrhea

- One of the most common causes of anovulation and loss of menstrual cycles is **hypothalamic amenorrhea**
- Changes in hypothalamic signals appear to be triggered by an E deficit
 E deficit → decrease in signals that lead to the secretion of LH and GnRH → prevent ovulation
- The onset of hypothalamic amenorrhea is related to being underweight, weight loss, or weight loss accompanied by intense exercise
- It is often preceded by menstrual irregularities lasting months to years

Nutritional management

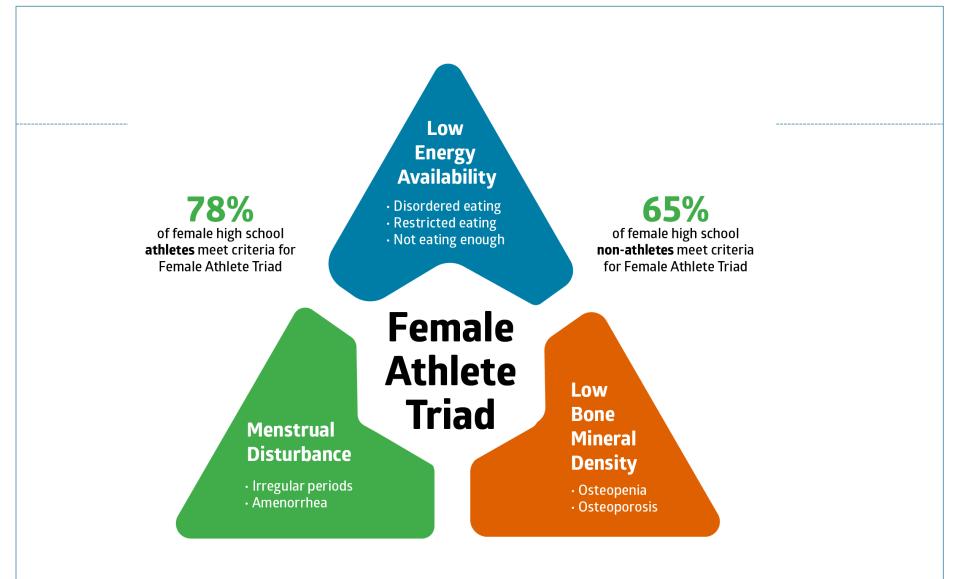
- First line of treatment: wt gain/ consumption of a healthy diet
- Wt gains of 3-5 kg are usually sufficient to restore fertility and improve the outcome of pregnancy
- Fertility can be restored in underweight and E deficient women by hormonal therapy
 - $\circ \uparrow$ risks of pregnancy and newborn complications and \uparrow health care costs with this approach

The female athlete triad and fertility

1. Disordered eating- effects E availability

2. Menstrual dysfunction:

- 1. Luteal suppression
- 2. anovulation
- 3. oligomenorrhea
- 4. primary and secondary amenorrhea
- 3. Impaired bone health- hormonal shifts result in ↓bone density and an ↑ susceptibility to stress fractures in affected athletes

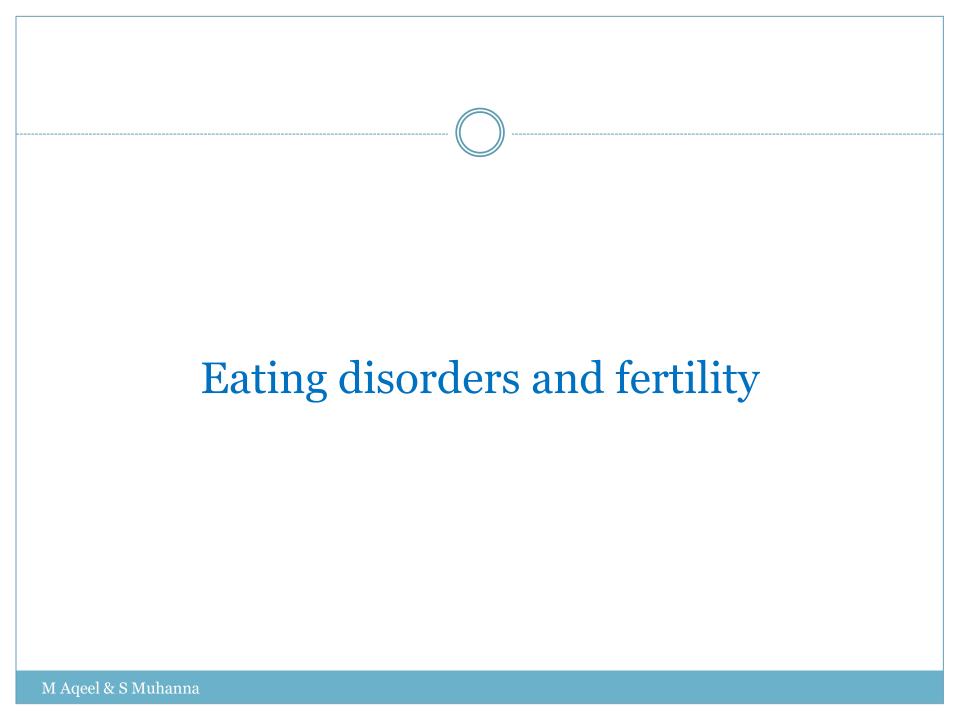


AlgaeCal

Source https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2848387/

Nutritional management

- Balanced diet → correct –ve E balance
- Restoration of bone mass
 - Vit D and Ca supplements may be required
- Treatment of any associated eating disorders



Anorexia Nervosa

• <u>A disorder characterized by:</u>

- Extreme underweight, malnutrition
- Amenorrhea: main manifestation of anorexia nervosa- related to irregular release of GnRH and very low levels of estrogen
- Low BMD: osteoporosis and short stature are potential long-lasting effects
- $\circ~$ Irrational fear of wt gain
- Restricted food intake
- Hyperactivity
- Disturbances in body image
- Menses generally returns upon wt gain, but some cases of infertility can persist even after normal wt is attained
 - This effect may be related to continued low levels of body fat, low dietary fat intake, excessive exercise

Bulimia Nervosa

• <u>A disorder characterized by:</u>

- Repeated sessions of uncontrolled, rapid ingestion of large quantities of food- binge eating
- Self-induced vomiting
- Laxative or diuretic use
- Fasting
- $\,\circ\,$ Vigorous exercise to prevent wt gain
- Feelings of disgust and guilt
- Food binges are related to low FSH and LH levels
- Menstrual disturbances, little bleeding during menses, amenorrhea, and infertility may occur

- Primary therapeutic goal for AN → normalization of body weight
- Primary therapeutic goal for BN→ normalization of eating behaviors



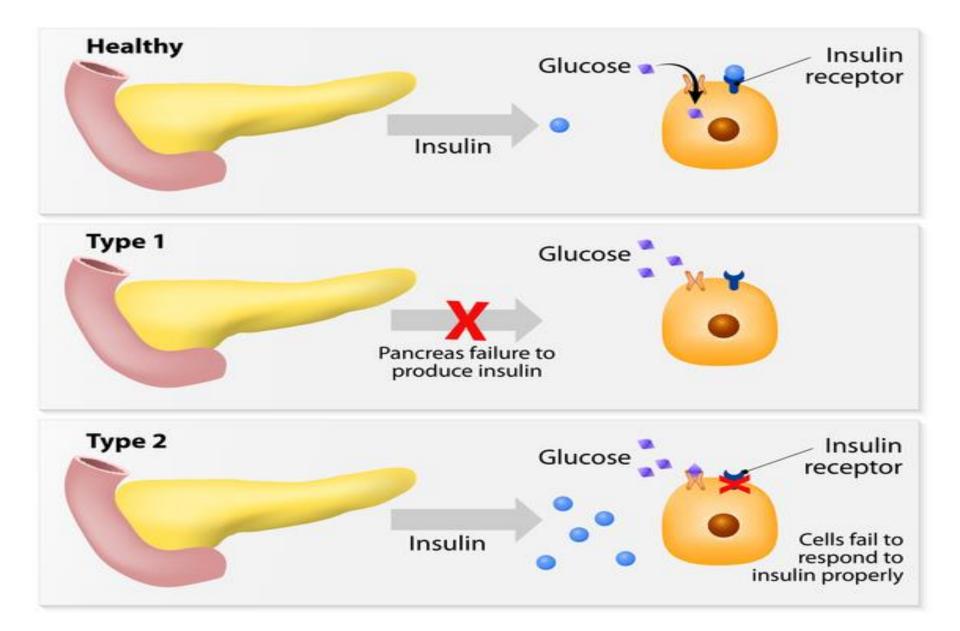
Diabetes mellitus prior to pregnancy

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Type I Diabetes A disease characterized by high blood glucose levels resulting from destruction of the insulinproducing cells of the pancreas. This type of diabetes was called juvenile-onset diabetes and insulin-dependent diabetes in the past, and its official name is type I diabetes mellitus.

Type 2 Diabetes A disease characterized by high blood glucose levels due to the body's inability to use insulin normally, or to produce enough insulin. This type of diabetes was called adultonset diabetes and non- insulin-dependent diabetes in the past, and its official name is type 2 diabetes mellitus.

DIABETES MELLITUS



Diabetes mellitus prior to pregnancy

- This disorder increases the risk of maternal and fetal complications
 - High blood glucose levels during the first two months of pregnancy are teratogenic
 - **2-3** fold increase in the incidence of congenital abnormalities
 - Fetal complications: macrosomia, acute hypoglycemia; increased risk of jaundice
 - Mother: Increased risk of miscarriage, preeclampsia and c-section
- Management approaches to blood glucose control in diabetes depends on the type of diabetes present

| Category | Fasting Plasma Glucose Test | 2-Hour Plasma Glucose Test | Hemoglobin A1c |
|----------------------------------|---------------------------------------|------------------------------------|----------------------|
| Normal | <100 mg/dL (<5.6 mmol/L) | <140 mg/dL (7.8 mmol/L) | <5.7% |
| Impaired Fasting Glucose | 100-125 mg/dL (5.6- 6.9 mmol/L) | | |
| Impaired Glucose Tolerance | | 140-199 mg/dL (7.8-11.0 mmol/L) | Prediabetes 5.7-6.4% |
| Diabetes | ≥126 mg/dL (≥7.0 mmol/L) | ≥200 mg/dL (11.1 mmol/L) | ≥6.5% |

Nutritional management of type I diabetes

• Goals:

- Control of blood glucose levels
- \circ Resolution of co-existing health problems
- Health maintenance

Nutritional management of type I diabetes

- Diets are controlled in carb content → control levels of BG and insulin secretion
- Consume foods low in GI and high in fiber- esp soluble fiber such as oatmeal
- Consume fruits and veggies, low fat meat and dairy products, fish, dried beans, nuts and seeds
- Reduced calorie diet plans should be included as part of the care for individuals with type 1 diabetes <u>who would benefit from wt loss</u>
- Physical activity- improves blood glucose levels, physical fitness, and insulin utilization
- RD- individualized meal and PA plans

Nutritional management of type II diabetes

- Can be managed through diet and exercise in some patients
- Others need medication- to increase insulin production or sensitivity

• Management includes:

- Individualized diet
- Exercise recommendations
- Education component
- Follow-up

American Diabetes Association Guidelines

- Wt loss \geq 7% of BW
- Macronutrient distribution: 15–20% protein, ,30% fat, ~ 50% carbs
- Calories from SF: 7%
- Calories from *trans* fat \rightarrow as low as possible
- Restriction of cholesterol intake to ≤200 mg/ day
- 14 g fiber/1000 calories of food intake
- Whole grains should comprise 1/2 of all grain intake
- Low GI foods
- Consumption of fish
 - 2-3 servings/wk- excluding commercially available fried fish fillet-or taking fish oil supplements→ lowers blood TG in people with elevated levels

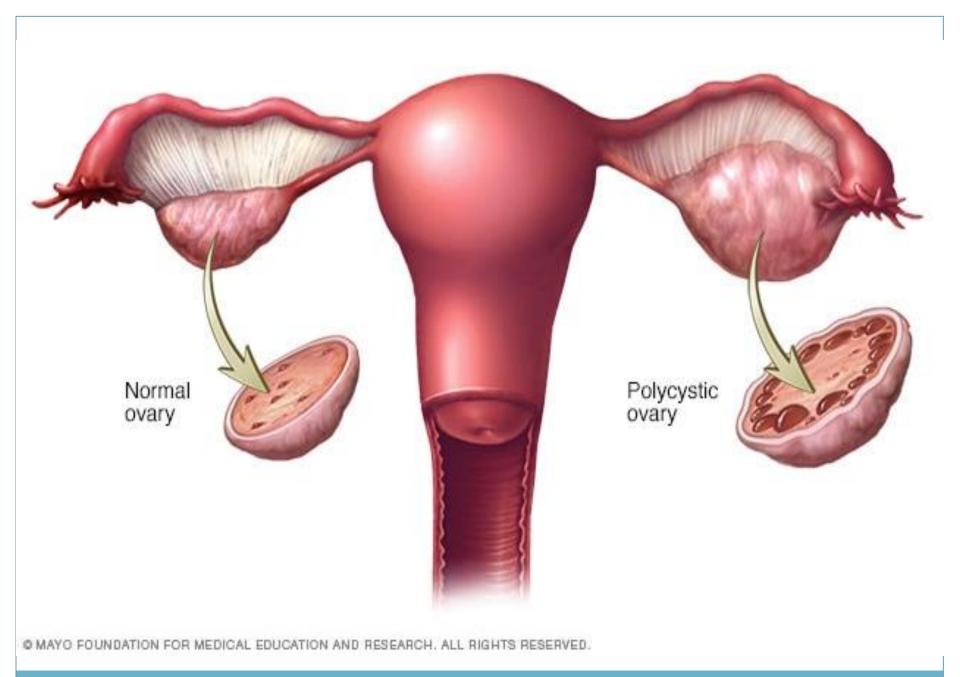
Prevention of Gestational Diabetes

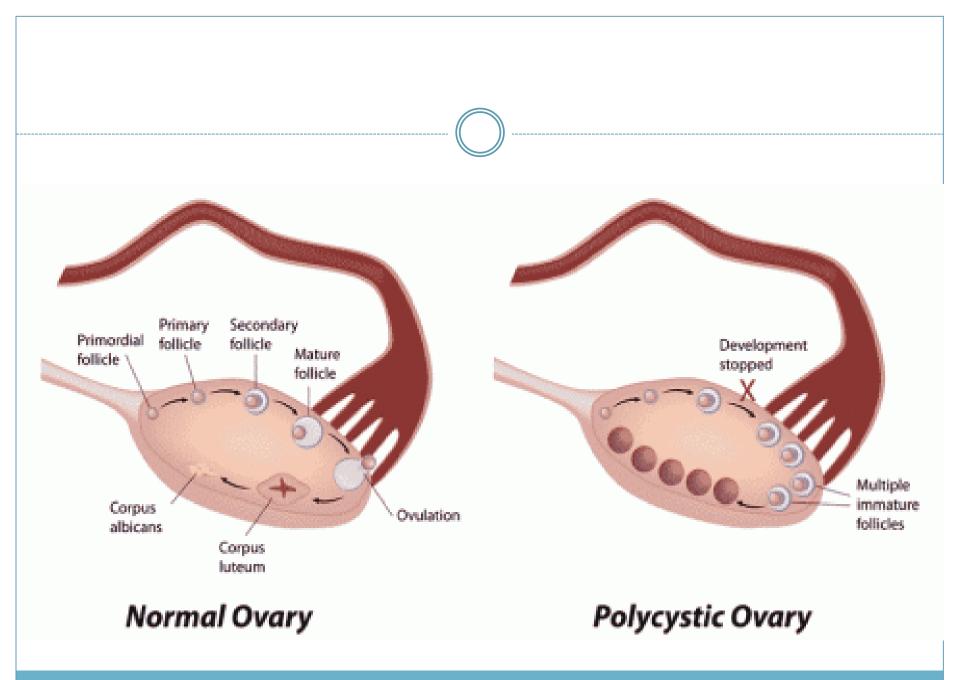
- It is a form of type 2 diabetes
- Weight loss if overweight before pregnancy (not recommended during pregnancy)
- Healthy dietary pattern
- Exercise

Polycystic ovary syndrome

• PCOS is a leading cause of female infertility

- Most women with PCOS are infertile due to the absence of ovulation, and they have menstrual irregularities
 - The outer layer of the ovaries is thick and hard, and it may look yellowish
 - Due to the hard covering on the ovaries, follicles cannot break open to release the egg





Many women with PCOS are obese or have high levels of intra-abdominal fat

Table 3.4 Variation in clinical signs associated

| | Percent of Women |
|-------------------------------|--------------------|
| Clinical Sign | with PCOS Affected |
| Menstrual irregularities | 90% |
| Polycystic ovaries | 67-86% |
| Excess abdominal fat | 80% |
| Insulin resistance | 80% |
| Overweight, obesity | 80% |
| Abnormal facial and body hair | 70% |
| High testosterone levels | 70% |
| Infertility | 70% |
| Low HDL-cholesterol levels | 64% |
| High triglycerides | 47% |

Cause of PCOS is still debated

- IR plays a vital role in most cases <u>regardless of BW</u>
- High blood insulin levels stimulate the ovaries to produce androgens e.g., testosterone→ excess disrupts development of follicles
 - High insulin levels raise TG and lower HDL-C levels
- Women with PCOS are at increased risk of spontaneous abortions, gestational and type 2 diabetes, HTN, and CVD

- Androgen secreting tumors in the ovaries or adrenal gland
- Use of certain medications
- PCOS & genetics
- Obesity does not cause PCOS but it can worsen reproductive and metabolic problems associated with it

The primary goal→ increase insulin sensitivity

- Insulin-sensitizing drugs, such as metformin, can be used to lower blood insulin levels and reduce the excess production of androgens by the ovaries
- Other drugs may be used to stimulate ovulation
- Should be used in conjunction with diet and exercise

• First-line treatment for women with PCOS:

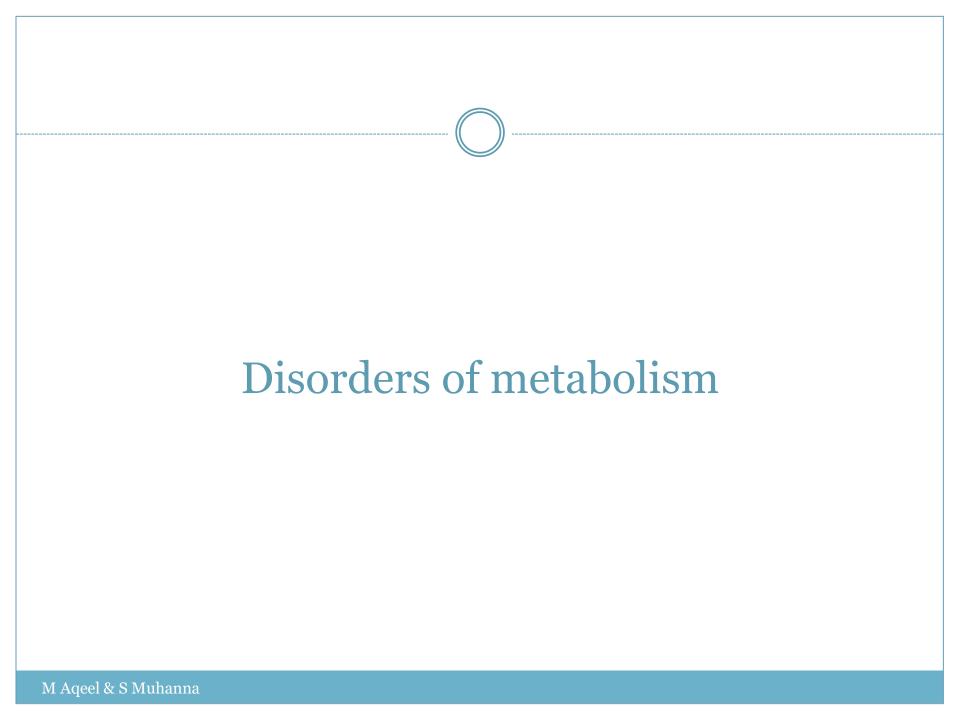
- o dietary modification, wt loss (if needed), and exercise
 - × Wt loss and exercise improve insulin sensitivity, benefit blood lipids and insulin levels, and lower fasting glucose and testosterone levels
 - × Symptoms of PCOS tend to improve substantially with wt loss of 5−10% of initial BW
- Individualize diet and exercise plans
- Education component

Dietary recommendations

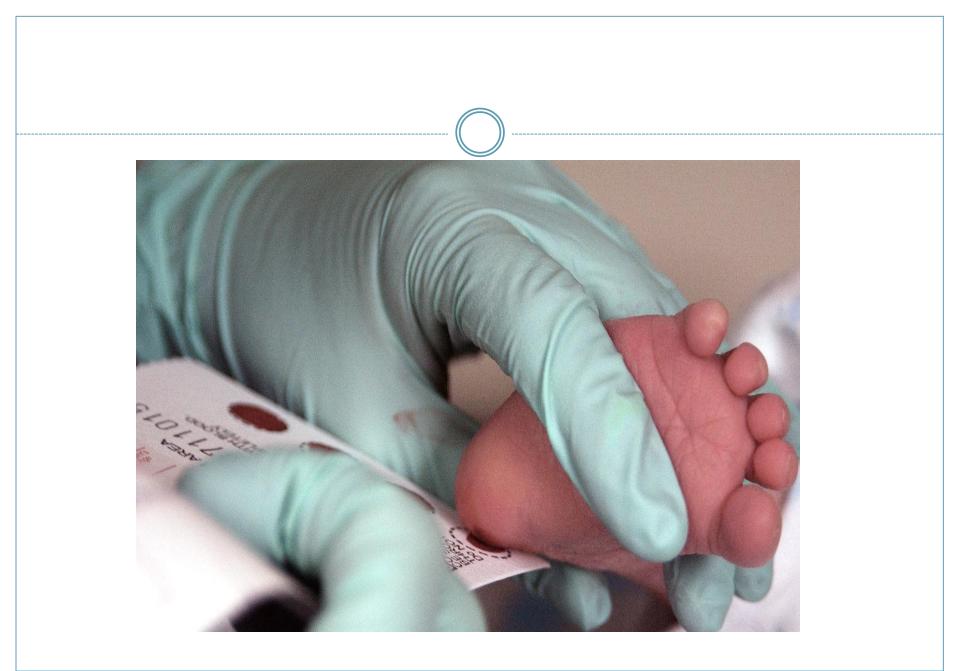
- Regular meals
- Marine sources of the omega-3FA- EPA and DHA→
 - $\circ \uparrow$ insulin sensitivity
- Whole grains
- Low-GI carbs

Limit BG surges and insulin production

- Fruits, and veggies high in antioxidants and fiber
- Nonfat dairy products
- Sweets should not be totally excluded



- An inherited-autosomal recessive- error in phenylalanine (Phe) metabolism most commonly caused by a deficiency of Phe hydroxylase
 - This enzyme converts EAA Phe \rightarrow tyrosine
 - Phe accumulates in the blood
- It is the most frequently inherited disorder of aa metabolism
- One of the few preventable causes of mental retardation



Phenylketonuria (PKU)

- If present during early pregnancy, high levels of Phe accumulate in the embryo and fetus and impair normal CNS development
- Elevated Phe levels in the first 8 weeks of pregnancy ↑ the risk of heart defects
- Consequences of untreated pregnant woman with PKU- on fetus:
 - Mental retardation
 - Microcephaly
 - Elevated risk of seizures
 - Hyperactivity
 - Abnormal behavioral patterns later in life

- Women who go off the PKU diet after childhood and become pregnant are at risk for a condition called "maternal PKU"
- Uncontrolled PKU in women represents risks for the fetus during pregnancy, even in fetuses that did not inherit the disorder
- The extent of the harm caused to the fetus increases with increased maternal Phe levels

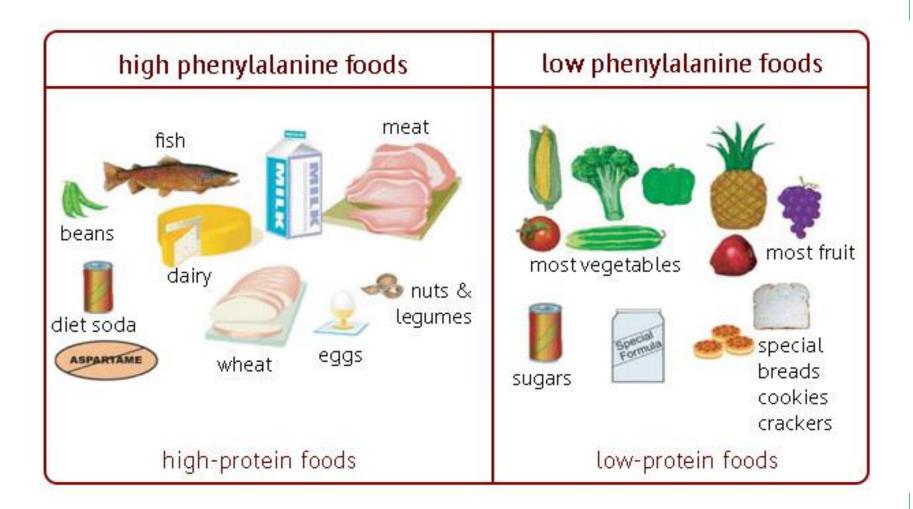
Maternal PKU

• Adverse effect on the fetus can be minimized if :

 maternal Phe levels are well controlled from the beginning of pregnancy

oE and nutrient needs of the mother are met

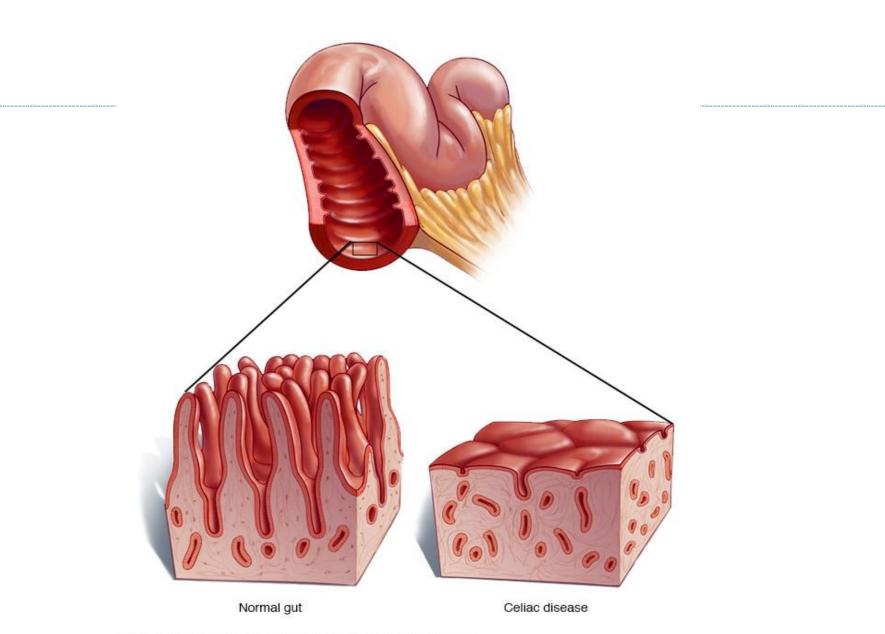
- Low-Phe diet
 - $\circ~$ Individualized based on blood Phe response to protein foods
- Maintain blood [Phe] in the range of 2–6 mg/dL
- High Phe protein foods such as meat, fish, eggs, and wheat are **excluded** from the diet
- Protein needs are met primarily though consumption of high-protein, low-Phe formulas and other formulated products
 - Formulated products are generally fortified with tyrosine, vitamins, and minerals
- Consumption of veggies, fruits, fats, sugars and high carb foods, and Phefree breads, flour, and pasta
- Milk is allowed if needed \rightarrow to maintain a minimal blood Phe level



Phenylketonuria (PKU)

- Infants born with PKU are started on low-Phe formula as soon after birth as possible
 - Individuals born with PKU who adhere to an adequate low-Phe diet throughout their lives <u>tend to develop normally</u> or <u>at levels that are</u> <u>somewhat below normal</u>
 - Life-long diet

- An autoimmune disease that causes malabsorption due to an inherited sensitivity to the protein gluten in wheat, rye, and barley
- *Hypothesis*: effects of disease on reproductive functions is related to malabsorption-induced deficiencies of nutrients including vitamins A, E, and D; folate, Zn and Fe, and direct effects of inflammation on intestinal and other tissues



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- <u>Males</u>: untreated celiac disease is related to alterations in the actions of androgens, delayed sexual maturation, and hypogonadism
 - Hypogonadism: marked by a deficiency of sex hormones and poor development and functioning of the reproductive system
- <u>Females</u>: untreated celiac disease is associated with amenorrhea, increased rates of miscarriage, fetal growth restriction, LBW deliveries, and a short duration of lactation

• <u>Goals:</u>

- Elimination of gluten from the diet
- \circ Correction of vitamin and mineral deficiencies
- Long-term maintenance of health
- **Gluten-free**: labeling term that indicates a product does not contain any species of wheat, rye, barley, or their hybrids, or ingredients that contain these grains, or \geq 20 ppm gluten- ~6 mg/serving
- Gluten is found in a variety of non-grain foods e.g., hot dogs, deli meats, some vitamin and mineral supplements, flavored potato chips...
- Normal reproductive functions return after celiac disease has been stabilized with a nutritionally adequate gluten-free diet

| 0 | |
|--------------------------------------|--------------------------------|
| Gluten-Containing Foods | Gluten-Free Foods ^a |
| Beer, ale | Fruit |
| Barley | Vegetables |
| Broth, bouillon powder/cubes | Dried beans |
| Brown rice syrup | Amaranth |
| Bulgur | Cassava, millet |
| Commercial soups, salad | Grits, corn, cornmeal |
| dressings Breads, cereals, pastas | Ouinea |
| | Quinoa |
| Imitation seafood | Oatmeal (gluten-free) |
| Cakes, pies, cookies | Fats |
| Processed meats | Fresh meats, fish |
| Soy sauce | Soy flour, cereals, tofu |
| Wheat starch | Rice, wild rice |
| Pizza | Eggs |
| Macaroni and cheese | Nuts, seeds |
| Seasonings | Cheese (not processed) |
| Marinades, gravies | Popcorn |
| Rye-containing products | Milks |
| Vegetarian meat substitutes | Chips (100% corn, |
| Flavored-rice packaged products | potato) |

Table 3.7 Examples of foods that do or do not contain gluten^{83, 94, 95}

^aAssumes foods have not been contaminated with gluten during processing and are free of gluten-containing ingredients.

Table 3.9 Key features of the Nutrition Care Process for individuals with celiac disease⁹⁹

A. Nutrition Assessment

- 1. Assessment of food/nutrition-related history
 - Food and nutrient intake with focus on vitamins and minerals listed in Table 3.5
 - Knowledge, skills, attitudes about celiac and dietary change
 - Access to food
- Assessment of biochemical data and medical results
 - Severity of intestinal lining damage
 - Presence of anemia, osteoporosis, other diseases

B. Nutrition Intervention

- Provide education and guidance on nutritionally adequate, gluten-free diet
- Advise on the use of gluten-free multivitamin and mineral supplement as required
- Provide resources and education on label reading, food cross-contamination, and support groups

C. Nutrition Monitoring and Evaluation

- Monitor dietary intake, gluten intake from all sources, celiac antibody levels
- Monitor persistent gastrointestinal symptoms not eliminated by a gluten-free diet, coordinate care
- Monitor nutrition risks for poor pregnancy outcomes



Herbal remedies for fertility-related problems: read from book