
بسم الله الرحمن الرحیم

Glucose Metabolism in Pregnancy

Carbohydrate metabolism

- Organs involving in maintaining blood glucose level
  - Liver
  - Muscle
  - Adipose tissue

Major hormones in CHO metabolism

- **Insulin**
- **Counterregulatory hormones :**
  - **Glucagon**
  - **Catecholamines**
  - **Cortisol**
  - **Growth hormone**

Glucose metabolism in normal pregnancy

- ✓ Pregnancy is characterized by a complex endocrine - metabolic adaptations, which don't reflect a pathological condition.

- ✓ These adaptations are necessary to ensure a continuous supply of nutrients & energy demands of the growing fetus and to prepare maternal organism for delivery & lactation.

- ✓ These metabolic adaptations are progressive & may highlighted in gestational diabetes mellitus (GDM).

Adaptations:

- ✓ Impaired insulin sensitivity
- ✓ Increased beta- cell response
- ✓ Altered blood glucose level
- ✓ Change in circulatory FFAs, TGs, CHOL & phospholipids.

Insulin Resistance (IR)

- ✓ During the first trimester of pregnancy, insulin sensitivity is normal if not higher than normal.
- ✓ As pregnancy progresses, a condition of IR come in progress.
- ✓ The deterioration of insulin action being more marked at the skeletal muscle than adipose tissue.

Insulin Resistance (IR)

- ✓ The development of GDM is associated with more severity of IR.
- ✓ In GDM mothers, a lower insulin sensitivity is likely to be present both before and after pregnancy.
- ✓ The degree of IR seems to be influenced by obesity & inheritance.

- ✓ According to other studies, with the progression of pregnancy, insulin sensitivity can be reduced as much as 60 to 80%.

Why insulin resistance?

A physiological event favoring glucose supply to the fetus.

- ✓ The reduced insulin-mediated utilization of glucose switches the maternal energy metabolism from carbohydrates to lipid substrates (free fatty acids), redirecting carbohydrates toward the fetal tissues.

Mechanism of insulin resistance in pregnancy

- The cellular mechanism of insulin resistance in pregnancy is ***multifactorial*** and involves several steps of the intracellular generation and propagation of the insulin signal.

Insulin Secretion

- ✓ Both in normal pregnancy and in GDM, insulin secretion increases steadily from the first trimester and reaches to its peak in the third, returning to normal values after delivery.

Hyperinsulinemia

- Increased circulating immunoreactive insulin in late pregnancy compared with non-pregnant women (intact form).
- Whole-body insulin kinetic are similar in pregnant & non-pregnant women.
- No difference in hepatic insulin extraction.

Hyperinsulinemia of pregnancy is due to enhanced pancrearic beta-cell function.

To satisfy these needs during normal pregnancy and in pregnancy with GDM:

The β-cell undergoes significant structural and functional changes including:

(1) increased insulin secretion

(2) increased insulin synthesis

(3) enhanced utilization and oxidation of glucose

(4) accelerated β-cell proliferation and increased islet volume

(5) higher cAMP metabolism

Insulin degradation

- Increased insulin degradation during pregnancy due to:
  - Placental enzymes with insulinase activity
  - Membrane- associated insulin-degrading activity

Hormones associated with modifications in insulin secretion and action

- ✓ **Estrogens** ↑ **Insulin concentration**
  ↑ **Insulin binding**

- ✓ **Progesterone** ↓ **Glucose transport**
  ↓ **Insulin binding**
  ↓ **Suppression of insulin- induced hepatic gluconeogenesis**

Continue:

- ✓ **Cortisol** → **↑ Insulin resistance**
  - **↓ Phosphorylation of insulin receptor**
  - **↓IRS-1**
- ✓ **placental hormones (hPL, GH)**
  - **↓ Insulin sensitivity**
  - **↑ Insulin secretion**
  - **↑ Insulin synthesis**
  - **↑ Utilization and glucose oxidation**
  - **↑ cAMP metabolism**
  - **↑ β-cell number**
  - **↑ β-cell mass**
- ✓ **Leptin** → **↑ Insulin resistance (?)**
- ✓ **Glucagon** → **↑ Insulin resistance**

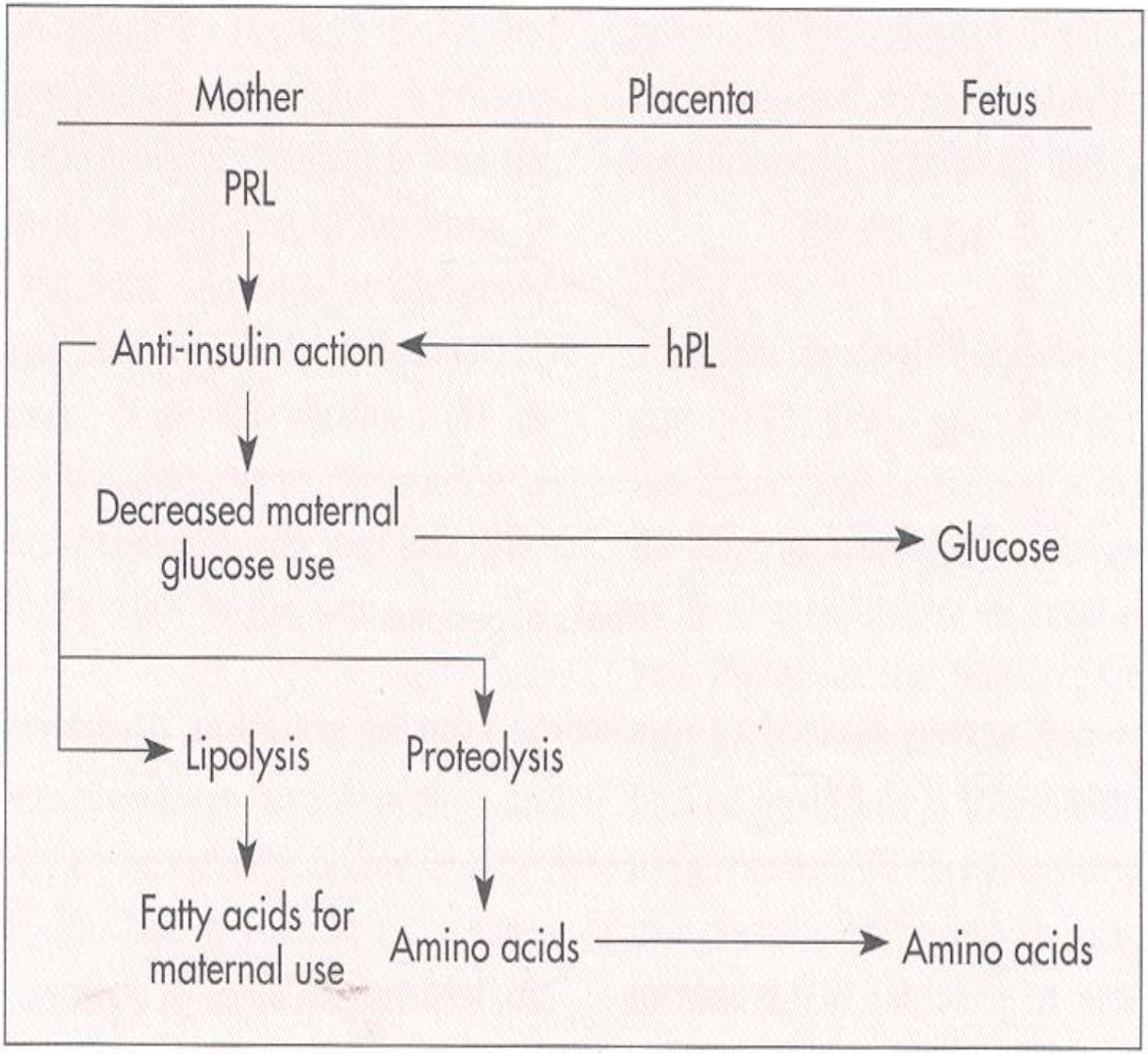

Figure 10-12 ■ Role of human placental lactogen *(hPL)* and prolactin *(PRL)* in altering maternal metabolism to provide amino acids and glucose to fetus.

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