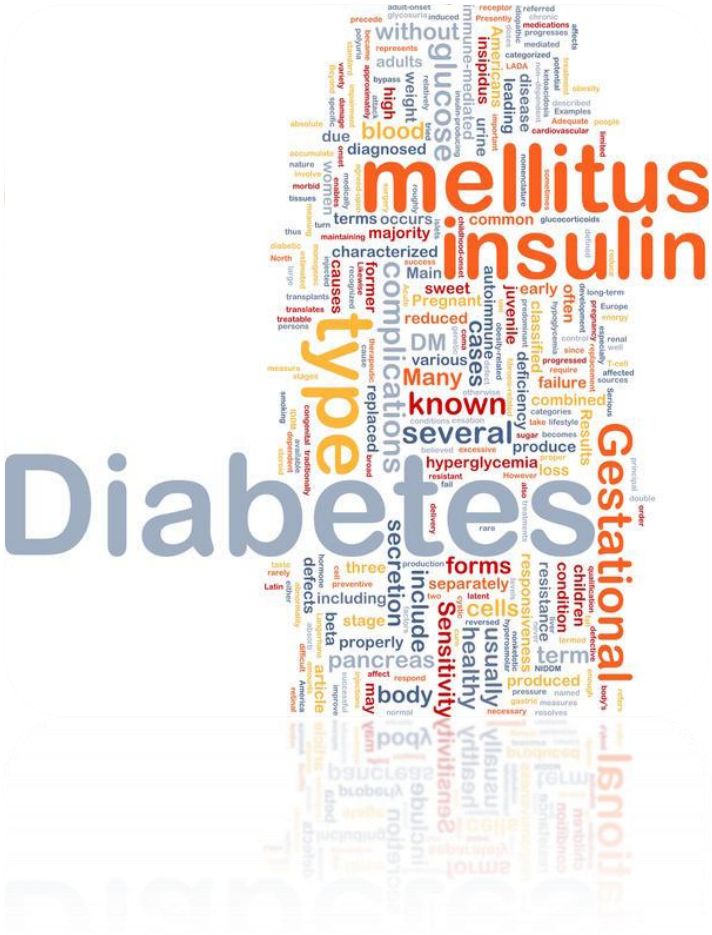

DIABETES IN PREGNANCY

429 OB/GYN TEAM NOTES

TEAM NOTES are in boxes

RESOURCES:

- *High-YieldTM Obstetrics and Gynecology 2nd Edition – Elmar P. Sakala*
- *Hacker and Moore's Essentials of Obstetrics and Gynecology International Edition*
- *Dr. Amel Al-Sayed slides*

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Diabetes in Pregnancy

	Gestational Diabetes	**Type 1 Diabetes** Early onset insulin dependent	**Type 2 Diabetes** Late onset insulin non dependent
Common Name	Pregnancy-induced	Juvenile-onset	Adult-onset
When Diagnosed	During pregnancy (Usually last half)	Onset prior to pregnancy	Onset prior to pregnancy
Mechanism	Insulin resistance	Pancreatic islet-cell destruction	Insulin resistance
Plasma Insulin Levels	High	Low	High
Therapeutic Modalities	Diet (15% need insulin)	Insulin Diet Exercise	Insulin Diet Exercise
How Diagnosed	2 or more abnormal values on a 3-hr 100g OGTT	Unable to achieve non-pregnant euglycemia without insulin	May achieve non-pregnant euglycemia without insulin
How Assess Success	- Home blood glucose - Monitoring (Blood sugar series)	- Home blood glucose - Monitoring (Blood sugar series)	- Home blood glucose - Monitoring (Blood sugar series)
Blood Glucose Target Values	FBS < 90 mg/dl 1-hr PP < 140 2-hr PP < 120	FBS < 90 mg/dl 1-hr PP < 140 2-hr PP < 120	FBS < 90 mg/dl 1-hr PP < 140 2-hr PP < 120
Increased Risk of Fetal Anomalies	None (because occurs after embryogenesis finished)	Possible	Possible
Fetal Growth Abnormalities	- Macrosomia - NO IUGR	- Macrosomia - IUGR (If small vessel disease)	- Macrosomia - IUGR (If small vessel disease)
Neonatal Hazards	**Hyper**bilirubinemia **Poly**cythemia **Hypo**glycemia **Hypo**calcaemia RDS (⇩ Surfactant)	**Hyper**bilirubinemia **Poly**cythemia **Hypo**glycemia **Hypo**calcaemia RDS (⇩ Surfactant)	**Hyper**bilirubinemia **Poly**cythemia **Hypo**glycemia **Hypo**calcaemia RDS (⇩ Surfactant)

GESTATIONAL DIABETES

DEFINITION

- A condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy (especially during *third trimester*).
- Carbohydrate intolerance that occurs in pregnancy after the 24th week of gestation.

GDM usually resolves after delivery but may include new onset of type I or type II DM.

INCIDENCE

- The overall incidence of diabetes in pregnancy is 3% (100,000 cases per year in the US).

RISK FACTORS

- A previous diagnosis of gestational diabetes or pre-diabetes (impaired glucose tolerance, or impaired fasting glycaemia).
- A family history of a first-degree relative with type 2 diabetes.
- Maternal age (>25 years).
- Obesity (>130% of IBW).
- Smoking.
- Polycystic Ovary Syndrome.
- A previous pregnancy which resulted in a child with a macrosomia.
- A previous pregnancy which resulted in a child with a birth weight > 4000g.
- Previous poor obstetric history; unexplained stillbirth, traumatic delivery and shoulder dystocia.

__Type 1 Diabetes on insulin__ is the type with the highest risk during pregnancy.

In managing __type 2 Diabetes__, oral agents may be used in the non-pregnant state but are contraindicated in pregnancy because of association with fetal/neonatal hypoglycemia.

OGTT: Oral glucose tolerance test, FBS: Fasting blood sugar,

2-hr PP: 2-hour Postprandial, RDS: Respiratory distress syndrome.

WHITE'S CLASSIFICATION OF DIABETES IN PREGNANCY

- This classification is helpful in assessing disease severity and the likelihood of complications.

CLASS	DESCRIPTION
A_1	Normal fasting in gestational diabetes.
A_2	Abnormal fasting in gestational diabetes.
B	Diabetes onset after age 20 years; duration < 10 years.
C	Diabetes onset age 10-19 years; duration 10-19 years.
D	Diabetes onset before age 10 years; duration 20 years or more.
F	Diabetes onset at any age; duration with nephropathy.
R	Diabetes onset at any age; duration with proliferative retinopathy.
H	Diabetes onset at any age; duration with arteriosclerotic heart disease.

MECHANISM

CARBOHYDRATE METABOLISM IN PREGNANCY

- Pregnancy is potentially diabetogenic.
- Diabetes maybe aggravated by pregnancy.

The diabetogenic effect of *Human Placental Lactogen (hPL)* is the most significant factor in GDM.

Placental insulinase, elevated free cortisol, & progesterone also act as mechanisms of glucose intolerance.

The hallmark of GDM is *increased insulin resistance*. Pregnancy hormones *(hPL)* and other factors are thought to interfere with the action of insulin as it binds to the insulin receptor. *Insulin resistance* prevents glucose from entering the cells properly. As a result, glucose remains in the bloodstream, where glucose levels rise.

- Because glucose travels across the placenta, in untreated gestational diabetes the fetus is exposed to consistently *higher glucose levels*.
- This leads to *increased* fetal levels of *insulin*.
- The growth-stimulating effects of insulin can lead to excessive growth and a large body (***macrosomia***).
- After birth, the high glucose environment disappears, leaving these newborns with ongoing high insulin production and susceptibility to low blood glucose levels (***hypoglycemia***).

NORMAL PREGNANCY IS CHARACTERIZED BY:

1. Mild fasting **hypo**glycemia, ↑ insulin level.
2. Postprandial **hyper**glycemia.
3. **Hyper**insulinemia.
4. Suppression of glucagon (role of glucagon in pregnancy is not fully understood).

WHAT ARE THE EFFECTS OF PREGNANCY ON DIABETES:

1. Insulin antagonism happens in pregnancy due to the action of hPL produced by the placenta as well as estrogen and progesterone ➔ difficulty in controlling diabetes.
2. ↑ Infection rate.

SCREENING

- 50 gm **Glucose Challenge Test (GCT)** between *24-28 weeks*.
  - Why do we screen for GDM between 24-28 weeks?
    Because that is the period of maximum Human Placental Lactogen (hPL), which is a diabetogenic hormone.
  - Procedure: A 50 gm oral glucose load is administered without the need for a fasting state. The test is performed at the first prenatal visit if patients meet risk criteria; otherwise, it is done between 24-28 weeks.
- Screening *Post-Partum* patients *who were diagnosed during pregnancy with GDM*, is done with 75 gm glucose at 6 weeks after delivery.

RESULTS

1. If the screening value is **140 mg/dl** or more, a 3-hr OGTT should be performed (the *diagnostic test* for GDM).
2. If the screening value is **200 mg/dl** or more, GDM is suggested.

> ✓ Glucose values above 140 mg/dl on a GCT are considered **abnormal** and have an 80% to 90% sensitivity in detecting GDM.
> ✓ An **abnormal** screening GCT is followed with a *diagnostic 3-hr OGTT*.

DIAGNOSTIC TEST FOR GDM

- The 3-hr 100 gm **Oral Glucose Tolerance Test (OGTT)** after 8 hrs of fasting.

- Procedure:
  - Checking the fasting blood glucose after an overnight fast.
  - Drinking a 100-g glucose drink, and checking glucose levels hourly for 3 hours.
  - The test should be performed after 3 days of unrestricted carbohydrate diet.

Screening: GCT

Diagnosis: OGTT

Three-hour Oral Glucose Tolerance Test	
Test	Maximal Normal Blood Glucose
Fasting	5.8 (95 mg/dl)
1 hour	10.6 (180 mg/dl)
2 hour	9.2 (155 mg/dl)
3 hour	8.1 (140 mg/dl)

- At least **2 values** have to be **abnormal**, regardless of which ones they are.

MCQ: You have to have **two** abnormal readings to diagnose GDM.

DIAGNOSIS

- Diabetes can be diagnosed for the 1st time during pregnancy.
- If diagnoses is prior to 24 weeks of gestation, this is ***overt diabetes*** and not gestational.
- Patients presenting with:
  - **Hyper**glycemia.
  - Glucosuria.
  - Ketoacidosis are easy to diagnose.
- Patients with mild carbohydrate metabolic disturbance need to be screened early based on the following risk factors: (as mentioned earlier)
  - Strong family history of diabetes.
  - History of giving birth to large infants.
  - Unexplained fetal loss.
  - Obesity.
  - Glucosuria which does not always indicate impaired glucose tolerance, but rather ↑ *Glomerular Filtration Rate* (GFR), nonetheless the detection of glucosuria in pregnancy mandates further investigations.
  - Age.
  - Previous history of GDM.

The "rule of 15s" applies to GDM:

1. *15% of gravidas have an abnormal GCT.*
2. *15% of gravidas with +ve GCT have an abnormal OGTT.*
3. *15% of GDM patients require insulin.*
4. *15% of GDM patients have macrosomic infants.*

MCQ: Blood sugar series, (in the hospital, after diabetic diet for 3 days at home):-

1. Fasting blood sugar.
2. Post-breakfast blood sugar.
3. Post-lunch blood sugar.
4. Post-dinner blood sugar.

COMPLICATIONS

MATERNAL COMPLICATIONS

- Preeclampsia / eclampsia: ↑ 4 folds, even in the absence of vascular disease.
- Polyhydramnios; leading to cardio-respiratory symptoms.
- Vaginal laceration; due to macrosomia.
- Bleeding from lacerations (Postpartum hemorrhage).
- ↑ incidence of C/S.
- ↑ rate of instrumental deliveries (e.g. forceps, and ventouse).
- ↑ the risk of having *type 2 DM* in the future.

FETAL AND NEONATAL COMPLICATIONS

- ↑ risk of sudden unexplained intrauterine fetal death.
- Macrosomia with traumatic delivery (e.g. Shoulder dystocia).
- Respiratory distress syndrome; due to incomplete lung maturation and impaired surfactant synthesis.
- **Hypo**glycemia (Persistent hyperinsulinemia from in utero hyperglycemia).
- Polycythemia (↑ Erythropoietin due to relative intrauterine hypoxia).
- **Hypo**calcemia (Immature parathyroid hormone function).
- **Hypo**magnesemia.
- Hyperbilirubinemia (Liver enzyme immaturity & ↑ breakdown of polycythemic RBCs).
- Jaundice.

Fetal hyperglycemia & hyperinsulinemia cause fetal overgrowth and macrosomia, which predisposes to birth trauma, including shoulder dystocia and Erb's' palsy.

➪ ***It is to be noted that congenital anomalies and abortion are NOT a risks with gestational diabetes.***

➪ *Anomalies are NOT increased because there is NO hyperglycemia during embryogenesis.*

➪ *Birth defects usually originate sometime during the **first trimester** (before the 13th week) of pregnancy, whereas **GDM** gradually develops and is **least** pronounced during the **first and early second trimester**.*

MCQ: Gestational diabetes is associated with an increased risk of all the following, EXCEPT:
A. Cesarean section.
B. Shoulder dystocia.
C. Fetal macrosomia.
D. Intrauterine fetal death.
E. Intrauterine growth restriction.

MANAGEMENT

1. PRENATAL CARE

A. Dietary Management

- The cornerstone is the American Diabetes Association (ADA) diet.

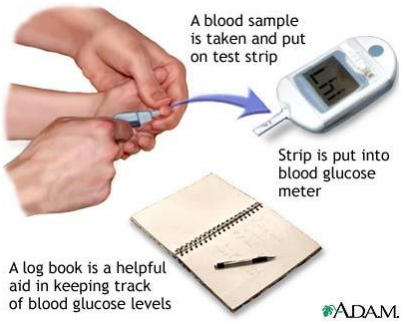
1) **Calories (generally 1800-2200 kcal/day)**
   a) Lean: 35 kcal/kg ideal pre-pregnancy weight (PPW).
   b) Obese: 25 kcal/kg ideal PPW.
2) **Composition**
   a) Carbohydrates: 50%-60% (complex, high fiber).
   b) Fat: 25%-30%.
   c) Protein: 10%-20%.
3) **Plan**
   a) Macronutrients and kilocalories should be spread evenly over 3 meals per day.
   b) There should be a bedtime snack.
   c) High-fiber foods should be encouraged.
   d) Sweets should be avoided.

Caloric intake is divided into: 25% at breakfast, 30% at lunch, 30% at dinner, and 15% at a bedtime snack.

B. Weight Management

1) **Steady, gradual weight gain** is more important than total weight gain.
2) **3rd trimester weight gain** should be 1 pound per week.

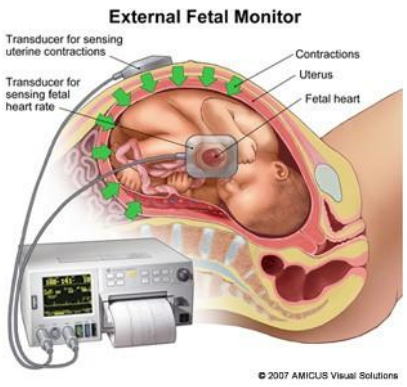
C. Management of ***Maternal Glycemic Control*** is the Central Goal



1) **Daily self-monitoring** of capillary blood glucose levels is performed, keeping a written record.
2) **Blood glucose target values** are:
   a) Fasting: <90 mg/dl.
   b) 1-hour post-meal: <140 mg/dl.
   c) 2-hour post-meal: <120 mg/dl.
3) **Outcomes**
   a) If the mother is normoglycemic, there is no increased risk of fetal jeopardy.
   b) If blood glucose values consistently exceed the target range, subcutaneous injection of long-acting and short-acting human insulin is prescribed.

➪ ***Oral hypoglycemics are contraindicated in pregnancy.***

D. Fetal Surveillance



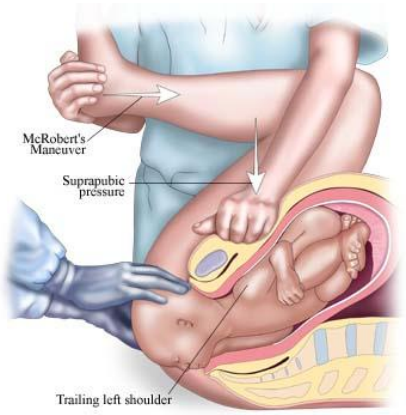
1) **If risk factors are present** (e.g. prior stillbirth, hypertension, preeclampsia and macrosomia), fetal well-being is not ensured. Twice-weekly NSTs (Non-Stress Test) and AFIs (Amniotic Fluid Index**)** should be started at 32 weeks.
2) **If no risk factors are present,** there is no risk of fetal jeopardy. Twice-weekly NSTs need not be started until 40 weeks.

2. DELIVERY AND POSTPARTUM MANAGEMENT

A. Delivery Management

1) **There is no need to induce labor** before 40 weeks' gestation in patients with glucose values in the target range.
2) **If pregnancy can't be controlled** and complications happened (e.g. retinopathy) → immediate admission.

3) **Induction of labor (IOL)** + **regular insulin** infusion + hourly checking of blood sugar during delivery.
    - **IOL** at completed **38 weeks** → for diabetics with insulin management.
    - **IOL** at term → for diabetics with diet management.
    - **Blood glucose levels** should be monitored during labor (maintain between 80-100 mg/dl).
4) **Macrosomia risk** should be evaluated clinically and by ultrasound.
    - A **C/S delivery** should be considered → if estimated fetal weight exceeds 4000-4500 g (4-4.5 kg).
5) The **risk of shoulder dystocia** rises with increasing birth weight. Appropriate management should include:
    - McRoberts maneuver (Sharp flexion of maternal thighs).
    - Suprapubic pressure → to disimpact anterior shoulder.
    - Wood's maneuver (Rotation of the anterior shoulder 180 degrees).
    - Delivery of the posterior arm and rotation of the anterior shoulder 180 degrees, bringing it posteriorly.



B. Neonatal Management

- Pediatric care should be available at the time of delivery.
- Infants should be observed for:
    - **Hypo**glycemia.
    - **Hypo**calcemia.
    - **Hyper**bilirubinemia.
    - Respiratory distress syndrome.
    - Polycythemia.

C. POSTPARTUM FOLLOW-UP

1) **Immediately after delivery**, observation for **postpartum hemorrhage** resulting from uterine atony → due to an over-distended uterus from a macrosomic infant.
2) **6 weeks after delivery** (or after completing lactation), **evaluation** for ***overt diabetes*** using the 2-hour 75 g OGTT.
    - Normal values are:

⇨ Fasting glucose < 126 mg/dl.
⇨ 2-hour GCT < 200 mg/dl.

DIABETES MELLITUS TYPE I & II

COMPLICATIONS

MATERNAL COMPLICATIONS

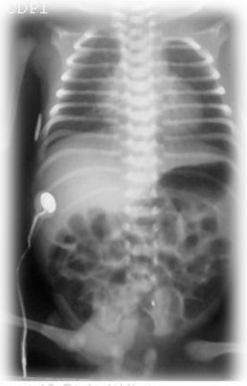
1. Preeclampsia / eclampsia.
2. Infections (e.g. Vaginal Candidiasis, UTI, endometrial or wound infection).
3. Injury to the birth canal 2^0 → due to macrosomia.
4. Bleeding from laceration (PPH).
5. ↑ incidence of C/S.
6. Polyhydramnios → leading to cardio-respiratory symptoms.
7. **Hypo**glycemia → due to high insulin intake.
8. Higher likelihood of diabetic ketoacidosis.
9. Nephropathy and retinopathy.
10. ↑ maternal mortality.

Increase susceptible of *diabetic ketoacidosis* in pregnancy because of:

- ☒ Increased excretion of bicarbonate will decrease buffering of Ketoacids.
- ☒ Decreased sensitivity of insulin due to antagonizing effect by cortisone, estrogen, progesterone, HPL, and degradation of insulin by placental insulinase.

FETAL AND NEONATAL COMPLICATIONS

1. ↑ risk of congenital anomalies; especially cardiac and CNS.
    - Sacral agenesis (most specific), an anomaly that occurs 200 times more often in diabetic women.
    - Congenital heart disease (most common) [e.g. Ventricular septal defect (VSDs), transposition of great vessels].
    - Neural tube defects (NTDs) [e.g. Anencephaly, Spina bifida].



2. ↑ risk of abortion.
3. ↑ risk of perinatal death.
4. ↑ risk of preterm labor.
5. Macrosomia may occur as a result of maternal hyperglycemia.
6. Asymmetric IUGR may occur as a result of placental insufficiency if the mother has small vessel vascular disease.
7. ↑ neonatal morbidity e.g.
    - Birth injury – Shoulder dystocia.
    - Respiratory distress syndrome.
    - Metabolic such as **hypo**glycemia.
8. Inheritance of diabetes or its predisposition.

MANAGEMENT

1. PRECONCEPTION AND PRENATAL MANAGEMENT

1) **Preconception counseling.** The overall goal is **prevention of congenital malformations** by achieving euglycemia at the time of embryogenesis:
    a) ↓ weight.
    b) **Exercise**; aerobic (e.g. brisk walking for about half an hour after meals).
    c) **Optimum glycemic control**.
    d) **Monitoring HbA_{1c}** (Glycosylated hemoglobin); to identify the average plasma glucose concentration over prolonged periods of time.
    e) **End-organ evaluation** should be performed.
    f) An **effective contraceptive program** should be established.
    g) **Rubella immunization** should be performed if the patient is susceptible.
    h) **Folate supplementation** of 4 mg/day should be initiated → to prevent fetal NTDs.

HbA_{1C} elevated values (>8.5%) should be targeted for careful ultrasonic assessment for congenital anomalies.

2) **End-organ evaluation** in pregnant women with insulin-dependent DM.
    a) **Renal status**.
        - Creatinine clearance should be measured twice during pregnancy.
        - Pregnancy should not worsen nephropathy.
    b) **Retinal status**.
        - A retinal examination should be performed twice during pregnancy.
        - Pregnancy does not worsen benign retinopathy, but it may increase active proliferative retinopathy.
    c) **Neuropathy**.
        - Altered autonomic response to hypoglycemia.
        - As well as to peripheral neuropathy and gastoparesis.
3) **Detection and evaluation of malformations**. Those with elevated first-trimester HbA_{1c} are at greatest risk.

- 13-14 weeks: **Sonography** → to rule out anencephaly.
- 16-18 weeks: **Triple-marker screen** → to rule out NTDs.
- 18-22 weeks: **Focused sonography** → to identify other structural anomalies.
- 22-24 weeks: **Fetal echocardiography** → to detect cardiac anomalies.

4) **Regulation of maternal glycemia**.
   a) **Glycemic goals**.
      - *Fasting*: 60-90 mg/dl.
      - *Before meals*: 60-105 mg/dl.
      - *2-hour post-prandial*: < 120 mg/dl.
      - *2-6 A.M.*: > 60 mg/dl.
   b) **Insulin therapy**.
      - The morning dose is two-thirds the total dose;
        2/3 am ➔ 2/3 NPH, 1/3 Reg.
        (Two-thirds NPH insulin, one-third regular insulin)
      - The evening dose is one-third the total dose;
        1/3 pm ➔ ½ NPH, ½ Reg.
        (One-half NPH insulin, one-half regular insulin)

Regular (rapid onset of action, short duration of action) & NPH (slower onset of action, longer duration of action).

5) **Fetal surveillance**.
   - **Ultrasound biometry** → to assess fetal growth.
   - **Maternal assessment of fetal activity** → begins between 26-30 weeks and continues until delivery.
   - **Twice-weekly NSTs** → starting at **32 weeks** with no risk factors, and at **26 weeks** with risk factors.

2. DELIVERY CARE IN PATIENTS WITH INSULIN-DEPENDENT DM

1) **Timing**.
   - Delivery can occur after 38 weeks' gestation if amniotic fluid analysis documents fetal pulmonary maturity.
2) **Intrapartum glycemic control**.
   - **IV** infusion + **regular insulin** + hourly **capillary blood glucose** measurements (target range 80-100 mg/dl).
3) **Postpartum glycemic control**.
   - Postpartum hypoglycemia can occur if the insulin infusion is not reduced after the placenta is delivered.

MCQ: During pregnancy, blood tests for diabetes are more abnormal than in nonpregnant state. This is due to:

A. Decreased insulin.
B. Increased absorption from the GI tract.
C. Increased placental lactogen.
D. Estrogen decreases and progesterone increases.
E. Hemoconcentration.

MCQ: Insulin requirements of pregnant diabetic women are greatest during:

A. The 1st half of pregnancy.
B. The 2nd half of pregnancy.
C. During lactation.
D. The immediate postpartum period.
E. None of the above.