PREGNANCY
Pregnancy

• Time of massive physical, psychological, emotional and social adjustment and change.

• Even women who strongly desire pregnancy are often ambivalent about its reality.

• Feelings of fulfillment and fears of failure are both very common.
Endocrinology of Pregnancy

- Fertilized ovum (zygote) begins producing Human Chorionic Gonadotropin (HCG) almost immediately after conception.

- HCG levels continue to rise during early pregnancy.
HCG

• Hormone measured in pregnancy tests

• Chemically very similar to LH

• Tests questionable in outcome until HCG levels are higher than LH ever gets in the cycling woman
HCG Role

• Transition hormone - keeps the corpus luteum alive until the placenta is functional as a hormone producing site.

• If the corpus luteum dies within 30-60 days after conception, the pregnancy will end in spontaneous abortion (commonly called a miscarriage).

• Corpus luteum typically lives throughout pregnancy but not critical for later pregnancy.
Placenta

• Derived from the fertilized ovum (now a blastocyst) and, therefore, genetically identical to the fetus not to the mother

Blastocyst

**Trophoblast** - develops into the placenta

Inner Cell Mass - Develops into embryo
Placenta

- Point of exchange of nutrients and waste products between fetus and mom.

- Transfer between mom and fetus is by diffusion across a concentration gradient.
  - Almost anything found in higher concentration in mom’s blood moves to the fetus’ blood and almost anything in higher concentration in the fetus’ blood moves into mom’s blood.

- No filters or barriers.
Umbilical cord

Mom’s blood

To fetus

Umbilical cord
Placenta

• Major endocrine gland of pregnancy

• Produces most of the estrogen and progesterone found in the woman during pregnancy

• Also produces a series of hormones similar to hormones produced by the anterior pituitary including HCG and Human Placental Lactogen
Human Placental Lactogen (HPL)

• Similar in structure to prolactin

• Works with estrogen and progesterone to:
  • 1. increase number of alveoli in mammary glands
  • 2. Make alveoli functional (capable of producing milk)
Estrial

• Made by the placenta
• Placenta CANNOT make estrial from cholesterol
• The placenta produces estrial from androstenedione that is produced by the fetal adrenal gland.
• Level of estrogen in mom’s blood is a measure of viability of the fetus.
Estrial Production (mostly pregnancy)

Cholesterol → Progesterone → Androstenedione → Estrial

Estrone, Testosterone, Estradiol
Actions of Estrogen during Pregnancy

- Stimulate the growth of the uterine muscle mass
  - increase size and strength needed for gestation and delivery

- Works with progesterone and HPL to stimulate growth of mammary glands
Progesterone

- Produced by the placenta from cholesterol.
- Cholesterol can come from mom.
- Level of progesterone during pregnancy can tell of the viability of the placenta but **NOT** the viability of the fetus.
Estrial Production
(mostly pregnancy)

Cholesterol

Progestosterone

Androstenedione

Estrial

Estrone

Testosterone

Estradiol
Actions of Progesterone during Pregnancy

- Inhibits coordinated contractions of the uterus
  - prevents early onset of labor

- Works with estrogen and HPL to stimulate the development of the mammary glands
Estrogen and Progesterone Levels in Pregnancy

- Both estrogen and progesterone increase rapidly during the first trimester of pregnancy.

- Slower climb but very high levels during 2nd and 3rd trimesters
Progesterone during Pregnancy vs. Monthly Cycle

• Monthly cycle
  • Day 1-14 (preovulatory phase): >1 to 1.5 ng/ml
  • Day 15-28 (postovulatory phase): 2-28 ng/ml

• Pregnancy
  • First Trimester: 9-47 ng/ml
  • Second Trimester: 17-147 ng/ml
  • Third Trimester: 55-200 ng/ml
Progesterone Levels during Monthly Cycle and during Pregnancy (ng/ml)
Embryonic development

Blastocyst

Inner Cell Mass
- Develops into embryo

Trophoblast - develops into the placenta
Embryonic Development

- Inner Cell Mass develops 3 layers:
  - **Ectoderm** – Central Nervous System, Peripheral Nervous System and Epidermis
  - **Mesoderm** – Skeletal System, Musculature, Vasculature
  - **Endoderm** – Gut, Lungs, Liver
Stages of Development

• 1\textsuperscript{st} trimester: Organogenesis
  • Rudimentary organs and structures laid down

• 2\textsuperscript{nd} trimester: Integration
  • Physiological structures begin to connect into systems and work together

• 3\textsuperscript{rd} trimester: Growth and Integration
  • Rapid increase in size and increased maturation of structures and systems
Thalidomide

- exception to the typical organogenesis toxin outcome (Typical outcome is death of embryo/miscarriage.)

- 1\textsuperscript{st} marketed in 1957 in West Germany

- Over the counter sedative but used by pregnant women to control morning sickness

- Use on specific days of the 1\textsuperscript{st} trimester resulted in phocomelia – failure to grow long limbs
Thalidomide

- Removed totally from market for decades

- Approved by FDA in 1998 and marketed as immunoprin, Talidex, & Thalomid for treatment of leprosy and multiple myeloma
Stages of Development

• 1\textsuperscript{st} trimester: Organogenesis
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Uterus During Pregnancy

- Most obvious change - increase in size of uterus
  - Muscle cells increase in size and number.
  - at term uterus is 6 times larger and 2000 times the capacity of non-pregnant uterus
  - Increased pressure of uterus on bladder = increased frequency of urination, one of the earliest symptoms of pregnancy
Uterus During Pregnancy

- Increase in the number of blood vessels and blood vessels increase in size.
- Much of the increase of weight of uterus during pregnancy due to increased blood flow.
Uterus During Pregnancy

- **Braxton-Hicks contractions**: irregular, painless contractions of uterus that begin in 1st trimester and increase in frequency and strength as pregnancy progresses.
Cervix during Pregnancy

- **Goodell’s Sign**
  - softening of cervix due to engorgement with blood
  - apparent by 6 weeks after conception

- Cervical mucus increases in volume.
- Mucus is thick and pasty. Forms a plug at the cervical os.
• In preparation for labor, the cervix effaces (disappears) and the os dilates (becomes wider).
Vagina during Pregnancy

• Lining thickens to strengthen walls.

• Blood supply to vaginal walls increases so that cells remain fresh and healthy.
Breast during Pregnancy

- Maximal development of mammary glands
  - result in breast tenderness and enlargement

- Increased vasculature

- May have darkening of areola and development of secondary areola (most visible in light-skinned individuals).
Breast during Pregnancy

• Montgomery glands more prominent.

• By 10th week, begin production of colostrum, a thin, yellow, high-protein substance (first nutrition for newborn)
Gastrointestinal System during Pregnancy

- Morning Sickness
  - experienced by 50-80% of all pregnant women
  - associated with hunger pangs
  - typically abates after 1st trimester

- Children of moms with severe morning sickness may display strong appetite for sodium in adulthood (Crystal and Bernstein, 1998)
Gastrointestinal System during Pregnancy

• Excessive salivation
  • also a first trimester event

• Heartburn
  • due to movement of partially digested food into the esophagus with weakened cardiac sphincter and pressure from uterus on stomach.
  • More common in 2nd and 3rd trimesters
Cardiovascular Changes during Pregnancy

- Blood pressure declines from pre-pregnant levels for first 22 weeks and then returns to pre-pregnant level.
High Blood Pressure during Pregnancy

• High blood pressure during pregnancy reflects a serious condition called toxemia.
  • Occurs in 6:100 pregnancies.
  • Can develop into pre-eclampsia (high blood pressure, edema, high urine protein levels).
  • Untreated pre-eclampsia can develop into eclampsia (convulsions, coma, even death for woman and fetus). 15-30% of maternal deaths worldwide are due to eclampsia.
Skeletal Changes during Pregnancy

- General softening of the ligaments of the sacroiliac and pelvis
  - allows joints to widen
  - reduces risk of broken bones during labor
- Changes induced by relaxin, a hormone produced by the corpus luteum and placenta
  - Relaxin levels highest in 3rd trimester
  - Results in changed gait during late pregnancy
CHILDBIRTH
Labor Onset

- Cause of labor onset: unknown!
- Seems to be a complex interplay between ongoing changes in several components: the baby, the uterus, and the placenta.
Late-Pregnancy Changes

**Baby**
- Stores iron
- Gains weight, fat, strength
- Secretes CRH and adrenal hormones

**Mother**
- Increased colostrum
- Pelvic joints relax
- "Nesting urge"
- Labor pain
- Rotation & Descent
- Pushing
- BIRTH
- Increased sensitivity to oxytocin
- Cervix ripens & effaces
- Progressing contractions
- Cervix dilates
- Rupture of membranes
- Decreased amniotic fluid
- Increased prostaglandin production
- Effects of increased estrogen surpass progesterone effects

**Uterus**
- Increased prostaglandin production

**Placenta**
- Fetal adrenal hormones converted to estrogen

Adapted from *Pregnancy, Childbirth, and the Newborn; Penny Simkin et al. (2010).*
Labor Onset: Hormones

• Drop in progesterone may allow for coordinated contractions of uterus

• Baby produces androgens that are converted to estrogen by placenta, which may help to increase uterine contractions.

• Oxytocin and prostaglandin levels high during labor and both can be used to stimulate labor
Common Signs that Labor has Begun

• Release of a small amount of blood mixed with mucus from the vagina

• Uterine contractions: frequent (intervals <10 minutes) and progressive (increasing in frequency and duration)

• Rupture of the amniotic sac (water breaking) – most often as a gush through the vagina, may be a slower leak.
Stages of Labor

- First Stage: divided in 3 phases
  1. **Latent phase** (longest phase; minimal discomfort; cervix at 3-5 cm)
  2. **Active phase** (contractions stronger and more frequent; cervix at 4-7 cm)
  3. **Transition** (cervix at 8-10 cm; strong and lengthy contractions)
Stages of Labor

• Second Stage – from the time the cervix is fully dilated until the baby has been delivered
  A. Pushing Stage
  B. Shorter than stage one – may take 30-120 minutes for first birth
Stages of Labor

- Third Stage – delivery of the placenta
  A. Lasts just a few minutes
  B. In some cultures, this is the most celebrated part of the birth process
Stage 1

Initial (Latent) Phase
- Fetus
- Uterus
- Cervix
- Vagina
- Umbilical Cord

Active Phase
- Fetus
- Uterus
- Effaced Cervix
- Vagina
- Umbilical Cord

Stage 2
- Fetus
- Uterus
- Umbilical Cord
- Crowning of the Head

Stage 3
- Placenta
- Cervix
- Umbilical Clamp
- Vagina
- Umbilical Cord
Breastfeeding - Lactation

- Immediately after birth, breasts continue to produce colostrum. Transition to mature breast milk takes about 30 days.
- Dependent on prolactin (for milk production) and oxytocin (for milk let-down).
Breastfeeding - Lactation

• Breastfeeding associated with improved health and growth of child - particularly true in areas where water is contaminated or formula is expensive.

• In Western societies, breastfeeding may result in slower weight gain and growth than formula feeding.
  • Could have long term consequences for body weight
Breastfeeding - Lactation

• Hormonal cyclicity and ovulation are unpredictable with lactation.

• If breast milk is only nutrition for child and child fed on-demand, round the clock, day after day, woman can remain non-cyclic and anovulatory for an extended period.
Breastfeeding - Lactation

• In the US, when mothers choose to breastfeed, children are breastfed for an average of 6 weeks.