Breast Structure & Presentation

- Present in both females and males
- **Boundaries:**
  - *Top:* 2nd rib
  - *Bottom:* 6th rib
  - *Medial:* sternum
  - *Lateral:* axilla
- **Supported by:** pectoral muscles, serratus anterior muscles, Cooper’s ligaments

Moore . et al. 2009
ILCA, 2008
Breast Structure & Presentation - External

- **Shape:**
  - Predominantly circular, except minor oblong part, which extends further into axillary region ("axillary tail")
  - Divided into 4 quadrants

- **Areola:**
  - Darkened area around nipples
  - *Glands of Montgomery*- small sebaceous glands
    - Produce sebum - oily substance
    - Enlarge during pregnancy and provide lubrication and protection to nipple
    - Antisepsis (?)

- **Nipple:**
  - Porous (not just one pore)
  - Terminal ends of milk ducts → deliver milk to baby
  - Both areola & nipple have erectile smooth muscles (also prevents leaking)

*Photo from NBCI*

Moore et al. 2009
Auerbach & Riordan, 2004
Breast Structure & Presentation - Internal

**Parenchyma (functional):**
- Glandular (w/ducts) – makes up 2/3 of the tissue under areola & nipple

**Stroma (supporting):**
- Adipose - interspersed throughout breast
- Cooper’s ligaments
- Blood vessels
- Lymphatics
- Nerves

Ramsay et al. 2005
Hale & Hartman, 2007
ILCA, 2008
**Blood Supply:**
- Intercostal arteries
- Internal Thoracic arteries
- Lateral Thoracic arteries

**Lymphatic Drainage:**
- Supra/sub clavicular
- Axillary Nodes
- Parasternal nodes

- Provide oxygen and nutrients
- Remove CO₂ and waste
- Hormones

- Return fluid to blood
- Immune system

Geddes et al. 2012
Moore et al. 2009
ILCA, 2008
Neuronal Pathways:

• Intercostal nerves (4, 5, 6)
• Communication with brain & spinal cord (Central Nervous System)
• Sensory (tingling, pain, etc...)
• Motor (nipples & areola)
  • No motor nerves found innervating alveoli → not associated with synthesis and secretion of milk??

Hale & Hartman, 2007
Glandular tissue

15-20 lobes

lobules

alveoli

lactocytes

Hartman & Hale 2007
Anatomy of Breast: Conventional View

Figure 2. A schematic diagram of the anatomy of the breast representing conventional anatomy. (Reproduced with the permission, copyright Medela AG.)

Hartman & Hale 2007

alveoli → small ducts → larger ducts → milk ducts (lactiferous sinus) → nipple

Auerbach & Riordan, 2004
Anatomy of Breast: **NEW!!**

**New imaging techniques show:**

- Fewer milk ducts (average 9; range 4-18)
- Milk ducts branch closer to nipple
  - 65% of glandular tissue within 30mm radius from base
- Milk ducts are small and do not display lactiferous sinuses (dilated portion beneath nipple)-only dilate with milk ejection reflex
- Milk ducts do not store large amounts of milk

*Hartman & Hale 2007*

*Ramsay et al. 2005*
Basic units of mature mammary gland:

**Alveoli**

- Where breastmilk is produced, stored and released
- Lined with *lactocytes* (secretory epithelial cells) that secrete milk
- Each cluster of cells is surrounded by a contractile unit of *myoepithelial cells* responsible for squeezing milk into ducts
- *Capillary network* supplies nutrients, hormones and substrates to lactocytes required for breastmilk synthesis

*Hartman & Hale 2007*

*Neville & Morton, 2001*
Milk ducts:
• Carry milk into nipple (transition from gland to nipple)
• Do not actively participate in secretion or modification of milk
• Also has inner layer of epithelium
• Also has layer of contractile myoepithelial cells on the outside (different shape than that of alveous)
• Shape may vary according to amount of milk present

Ramsay et al. 2005

Hartman & Hale 2007
Mammary Secretory Cell: Lactocyte

- Secretory epithelial cells
- Junctions between cells-tight (closed) during lactation, but are leaky (open) in the non-lactating & pregnant breast
- Luminal side is **apical** (where secretion occurs)
- Outer side is **basal** (where materials are taken up from blood)

*Hale & Hartman, 2007*
Mammary Secretory Cell: Lactocyte

**Secretory mechanisms:**

- **Exocytosis:** most proteins, lactose, citrate
- **Transcytosis (endocytosis+exocytosis):** immunoglobulin (Ig)
- **Droplets:** fat
- **Diffusion/Osmosis (sometimes w/ transporter):** water & ions
- **Paracellular (b/w cells):** white blood cells & water soluble compounds

McManaman & Neville, 2003
What are the major constituents?

- **Protein**: transported from circulation and ingested by lactocyte or made in the lactocyte from amino acids (building blocks for protein)
  - examples of proteins: Ig, milk protein, hormones, growth factors, enzymes

![Diagram of mammary secretory cell with amino acids, milk protein, and IgA, other proteins highlighted.](image-url)
What are the major constituents?

- **Carbohydrates**: lactose makes up 98% of carbohydrates in breastmilk
  - Glucose & galactose (building blocks for lactose) are transported into lactocyte and lactose is made there
What are the major constituents? (cont’d)

- **Fat:** provides 1/3 of the breastmilk calories
  - Also important for delivery of essential fatty acids & fat soluble vitamins (ADEK)
  - *Short fatty acids* made in the lactocyte
  - *Long fatty acids* imported from blood (dietary or made in adipose tissue)
- Secreted in droplets w/ lipases to help digest

![Diagram of fatty lipids]
What are the major constituents? (cont’d)

- Metabolites & Ions: e.g. citrate, sodium, potassium, calcium
- Living cells: e.g. white blood cells (leukocytes), stem cells
BREAK
Development

- human mammary system is unique in that it changes dramatically from birth through puberty, pregnancy and lactation
- no other organ changes so much in size shape and function.

**Fetal:**

- 3rd-4th week of gestation: development of primitive milk streak
- 6th week: development of milk line
- 7th weeks: mammary disc & primitive blood vessels formed
- 10-12 weeks: formation of epithelial buds
- 16 weeks: mammary vascular system completely formed
- 20 weeks: solid cords (ductal structures) formed
- 32-term: primary milk duct and alveolar development (canalization)
  - development of external nipple and areola
- After birth, neonatal mammary tissue may secrete colostrum ("witches milk")

*ILCA, 2008*
Prepubertal:

- Rudimentary ductal system
- Development is general until puberty (grows proportionally to rest of body)

Puberty:

- **Estrogen** is major influence of breast growth (mainly adipose tissue)
- Rudimentary ducts grow and divide forming extensive ductal network
- Proliferation and growth of epithelial tissue occurs with each cycle until ~35 yrs
- **Hormones involved**: Estrogen, prolactin, LH, FSH and growth hormone
- Only during pregnancy does complete functioning of mammary gland develop

*ILCA, 2008*
Pregnancy and Hormonal Involvement

External Changes (variable):
- Breasts enlarge (more glandular tissue)
- Skin appears thinner and veins become more prominent
- Diameter and pigment of areola increases
- Nipples become more erect and Montgomery glands enlarge

Auerbach & Riordin 2004

Mammogenesis: 1st half of pregnancy
- Rapid and extensive ductal branching and lobular formation (increased breast tenderness)
- Decreased adipose tissue?
- Increased epithelial cells → proliferation of alveoli
- Full differentiation of lobules (i.e. maturation)
- Influenced by estrogen, progesterone, prolactin, human placental lactogen, growth hormone, insulin-like growth hormone, etc...

Cregan & Hartmann 1999
Pregnancy and Hormonal Involvement

Lactogenesis I: 2nd half of pregnancy (16-18 weeks)

- Differentiation of epithelial cells into lactocytes
- Synthesis of milk specific components secreted into lobules and ducts
- Early milk secretion = colostrum

- Influenced by estrogen, progesterone, prolactin, oxytocin, growth hormone, insulin, glucocorticoids, thyroid-parathyroid hormone

Auerbach & Riorden, 2005
Hale & Hartman, 2007
ILCA, 2008
Postpartum and Hormonal Involvement

**DELIBERY:**

- Estrogen and progesterone levels fall dramatically
- Disinhibits the effect of *prolactin and oxytocin*

➢ **Lactogenesis II**

- Onset of *copious* milk production
- Triggered by withdrawal of progesterone - removes inhibition of prolactin
- Closure of tight junctions ➔ increased rate of milk secretion
- Prolactin triggers lactose synthesis (via *alpha lactalbumin*) ➔ draws water into secretion ➔ contributes to increased volume

*Neville & Morton, 2001
Cregan & Hartmann 1999*
Lactogenesis III (aka glactopoiesis)
- Once lactation is established, milk secretion regulated by milk removal and hormone release
- Early and frequent breastfeeding (effective milk extraction) may increase number of prolactin receptor cells → increased milk production???

Involution
- Occurs once feeding or expression ceases
- Trigger:
  - pressure from distended gland and cessation of stimulation (?)
  - Feedback Inhibitor of Lactation (FIL) slows milk synthesis when breast full
- Re-opening of junctions (become leaky)
- Milk stasis/accumulation leads to apoptosis (cell death) of lactocytes
- Decreased hormones
Postpartum: Key Players

**Prolactin:**
- Suckling at the breast stimulates *anterior pituitary* to secrete prolactin
- Stimulates lactocytes of alveoli to secrete milk (“fill up”)
- High prolactin levels may suppress ovulation in mother

- *Prolactin Inhibiting Factor* (e.g. dopamine) secreted from the hypothalamus inhibits prolactin secretion

**Oxytocin:**
- Suckling at the breast also stimulates *posterior pituitary* to secrete oxytocin
- Causes contraction of myoepithelial muscles around the alveoli → squeezes milk into ducts
  - Ducts dilate 2X resting diameter
- “milk ejection”/ “let-down” reflex

*Neville & Morton, 2001
Auerbach & Riorden, 2005
Hale & Hartman, 2007
ILCA, 2008*
Summary of Hormonal Pathways

- Oxytocin
  - Stimulate myoepithelial cells to eject milk into ducts

- Prolactin
  - Stimulate lactocytes to secrete milk

- Dopamine
  - Inhibits prolactin release
  - Stimulation of distended glands or presence of FIL

- Milk supply
  - Increased with prolactin and oxytocin stimulation
Lactation Cycle (what’s happening in the alveoli?)

- Empty
- Filling
- Full
- Milk Removal
- Resting
- Recruitment
- Involution

Adapted from Molenaar et al. 1992
What is a Normal Breast?

- Breast size vary in size, shape, colour and placement between women
- Asymmetry is common
- Supranumery nipple tissue may occur at any point along the milk line from axilla (armpit) to groin

Photos from NBCI
What is a Normal Breast?

• Does size matter?

Photos from NBCI
What is a Normal Breast?

• Flat nipples?

Photos from NBCI
Anomalies of Anatomy and Physiology

• Mammary hypoplasia: insufficient growth and development of breasts

• Insufficient glandular tissue

• Retained placenta

• Damage to anterior pituitary (sudden drop in BP, postpartum haemorrhage)

Photos from NBCI
Anomalies of Anatomy and Physiology

• Hormone disorders (low progesterone, high estrogen/testosterone, low thyroid)
• Anaemia
• Breast cancer
• Breast surgery: reduction, augmentation, lift, abscess

Photos from NBCI


Kent JC, Mitoulas LR, Cregan MD, Ramsay DT, Doherty DA, Hartmann PE. Volume and frequency of breastfeedings and fat content of breast milk throughout the day. Pediatrics. 2006; 117(3):387-95


Assignment

All answers should be typed or printed legibly. Point form is acceptable. Each answer should be no more than 500 words. Please cite all references.

1. Please discuss three maternal conditions that can delay or impair lactogenesis (particularly II & III). They may include birthing practices, chronic hormonal conditions, stress, etc...

2. Knowing how prolactin and the mechanisms inhibiting it affect lactation, how would modulators like domperidone work to increase milk supply?

3. Based on the “Lactation Cycle” (slide 28) and the article on Kent et al. 2006, what would you advise breastfeeding families with regards to feeding frequency, duration of feeds, and fat content (“foremilk vs. hindmilk”).