Objectives

- Define compounding and be familiar with its applicable standards and laws
- Review the difference between compounding and manufacturing
- Recognize compounding tools and vocabulary
- Define BHRT and the differences that set it apart from HRT
- Explain the roles for various hormones in treating female hormone deficiency

Per Alaska State Board of Pharmacy

- “Compounding means the preparation, mixing, assembling, packaging, or labeling of a drug or device (A) as the result of a practitioner’s prescription drug order or initiative based on the relationship of the practitioner, patient, and pharmacist in the course of professional practice or (B) for the purpose of, or as an incident to, research, teaching, or chemical analysis and not for sale or dispensing; “compounding” also includes the preparation of drugs or devices in anticipation of prescription drug orders based on routine, regularly observed prescribing patterns”

Compounding Standards

- USP <795>, USP <800>
- USP <797>
- Pharmacy Compounding Accreditation Board
- State Law and Regulation for compounding
- Federal Law for manufacturing
Alaska’s Good Compounding Practices

- Compounding in an amount above the historical basis is **manufacturing**
- “Not commercially available”
- Distribution of inordinate amounts of compounded products without the triad is **manufacturing**
- Pharmacist shall maintain proficiency through awareness and training
- Maintain records of formulas and procedures
- Stock products need proper labeling

Differences between manufacturing and compounding

<table>
<thead>
<tr>
<th>Manufacturing</th>
<th>Compounding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical trial to demonstrate efficacy</td>
<td>Patient specific prescription</td>
</tr>
<tr>
<td>Must submit new drug application (NDA)</td>
<td>Unique product</td>
</tr>
<tr>
<td>Must adhere to good manufacturing practices (GMPs)</td>
<td>NDA and GMP exempt</td>
</tr>
<tr>
<td>Promote product</td>
<td>Product promotion restrictions</td>
</tr>
<tr>
<td>Resale by others</td>
<td>Cannot be resold by others</td>
</tr>
</tbody>
</table>

Compounding Tools...

... and more Compounding Tools...

... and then which tool?
... improperly used Compounding Tools

Compounding Vocabulary
- Triturate (verb and noun!)
- Levigate
- EMP
- Syringe to syringe
- Geometric proportions
- Pack stats
- CofA, MSDS

More Vocab?!
- Alligation
- Aliquot
- pH
- Isotonicity
- QSAD
- mEq
- Molar
- Periodic table of elements

AND Extra Math?!

Compounding Dosage Forms
- Triturate
- Troche
- Suppository
  - Rectal suppository
- Cream, gel, ointment
- i.e. Bi-Der (B:2); estradiol 80%, estradiol 20%
- Phospholipid Organogel (PLO)
- Capsule – enteric coat, slow release
- Animal treat
- Suspension/solution
- Powder
- Rapid Dissolve Tablet (RDT)
- Lollipop
- Mucosal bandage
Disease States

ANY AND ALL! No boundaries
- Hormone replacement: Extra topic for today!
- Pain management
- Pediatric
- Veterinary
- Hospice
- Wound care
- Dental
- Sports medicine

Compound #1

- Script: Progesterone IR 100mg capsule, #25 caps
- Formula given:
  - Progesterone USP, ultra-micronized 2.5g
  - Avicel 1.425g
  - #3 capsules, clear-locking gelatin 25caps
- Directions given:
  1. In a mortar and pestle triturate powders using geometric proportions until homogeneous.
  2. Encapsulate step 1 into size 3 capsules.
  3. Label and dispense in amber plastic bottle.
- Quality assurance – MATH!!

Compound #1, cont.

Quality Assurance Math!
- Add all ingredient weights
  - Progesterone + Avicel + capsules
  - 2.5g + 1.425g + (25cap*0.046g/cap) =
- Find weight of one capsule
  - Total weight/total # of capsules
  - 3.925g/25caps =
- Find acceptable weight range
  - For 5% error: (0.157g*0.95) to (0.157g*1.05) =
  - For 10% error: (0.157g*0.9) to (0.157g*1.1) =

Compound #2

- Script: Bi-Est (8-2) 2.5mg/ml cream, 30ml
- Formula given:
  - Estriol USP powder 0.06g
  - Estradiol 1:10 aliquot 0.015g
  - Propylene glycol liq 0.2ml
  - Vanicream 29g
- Directions given:
  1. On ointment slab wet powders with propylene glycol and levigate to form a smooth paste.
  2. Incorporate vanicream into step 1 using geometric proportions and levigate until homogeneous.
  3. Label and dispense in ointment tube.
- Quality assurance

Compound #2, cont.

Extra Calibration Math
- How much cream base do we need to weigh?
- Knowns:
  - Powder displaces 70% of its weight in volume
  - Cream base density is 0.978g/ml
- Convert ingredients to ml
  - Estriol + Estradiol: (0.066g+0.165g)*0.7 =
  - Propylene glycol: 0.22ml
- Subtract from total volume
  - 33ml – (0.1617ml+0.22ml) =
- Convert volume needed of cream base to weight
  - 32.62ml*(0.978g/ml) =

Myth or Fact?

- We are to feel poorly as we age
- PMS is normal — women are CRAZY
- Menopause agony is normal — women are STILL CRAZY
- All hormones are created equally and are all evil
- Progesterone treatment is only for menopausal women WITH a uterus
- Progesterone = progestin
- Estrogen treatment increases breast cancer risks
Changing Perspective

- Superior doctors prevent disease
- Mediocre doctors treat impending disease
- Inferior doctors treat actual disease
  ~ Chinese Proverb

- The art of healing comes from nature, not from the physician. Therefore the physician must start from nature, with an open mind.
  ~ Paracelsus

Hormonal Balance

Female Hormone Imbalance

- Menopause
  - No menses for 1 year
  - Considered normal between ages 40-55
  - Adrenal glands take over hormone production
- Perimenopause
  - 5-10 years surrounding menopause
- Pre-menopause/Estrogen dominance
  - Imbalances of hormones pre-menopaually may contribute to variety of symptoms
  - Effects of too much estrogen relative to progesterone
    - Xenoestrogens: parabens, phthalates, BPA

Female Hormone Imbalance

- Predominantly estrogen >> progesterone
- Estrogen is a proliferative hormone
- Progesterone has “anti-estrogen” properties
- May start earlier in life as PMS
- Multiple factors play into imbalance
  - Cholesterol medication
  - Xenoestrogens
  - Oral contraception
  - Genetics
  - Diet
  - Weight gain/loss

Menopause Symptoms

- Hot flashes
- Night sweats
- Vaginal dryness
- Anxiety
- Mood swings
- Irritability
- Insomnia
- Depression
- Memory lapses
- Frequent urination
- Urinary leakage
- Loss of sexual interest
- Hair growth on face
- Painful intercourse
- Panic attacks
- Urinary tract infections
- Bloating
- Osteoporosis
- Hair loss
- Varicose veins
- Weight gain
- Indigestion

Pre-menopause/Estrogen Dominance

- Allergies
- Anxiety
- Autoimmune disorders
- Breast cancer
- Breast tenderness
- Insomnia
- Decreased sex drive
- Increased blood clotting
- Bloating
- Early onset of menstruation
- Endometrial cancer
- Fat gain, esp. hips/thighs
- Fibrocystic breasts
- Gallbladder disease
- Headaches
- Uterine fibroids
- Irregular menses
Female Menstrual Cycle

BHRT Defined

- **Bioidentical Hormone Replacement Therapy (BHRT)**
  - Hormone with same chemical structure as those made by the human body
  - Natural and synthetic
  - Derived from natural source; modified to look identical to human hormones
  - Metabolized by normal metabolic pathways
  - Means less harmful metabolites decreasing risk of side effects

HRT Defined

- **Hormone Replacement Therapy (HRT)**
  - Synthetic – non-bioidentical
  - Any combination of hormones – includes birth control
  - Manufactured with altered chemical structure to what human body makes
  - Prone to side effects
    - Bind tightly to receptors
    - Prolonged stimulation of receptors

HRT vs. BHRT

<table>
<thead>
<tr>
<th>SYNTHETIC</th>
<th>BIOIDENTICAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Different chemical structure</td>
<td>Same chemical structure</td>
</tr>
<tr>
<td>Prone to side effects</td>
<td>Less side effects</td>
</tr>
<tr>
<td>Less compliance</td>
<td>Better compliance</td>
</tr>
<tr>
<td>Increased risk of breast cancer</td>
<td>Decreased risk of breast cancer</td>
</tr>
<tr>
<td>Patentable</td>
<td>Non-patentable</td>
</tr>
<tr>
<td>Profit-driven $$$</td>
<td>Patient-driven</td>
</tr>
</tbody>
</table>

Women’s Health Initiative

- Instilled the FEAR of hormones!
  - First long-term study of HRT
  - Stopped prematurely
    - Increased risk of breast cancer, heart disease, stroke, blood clots
  - Limited to menopausal women – average age 68
  - 3 treatment groups
    - No treatment
    - Synthetic estrogen only
    - Synthetic estrogen + progestin
**Women’s Health Initiative**

- Synthetic estrogen vs. placebo
  - Decreased risk of breast cancer
- Synthetic estrogen + progestin vs. placebo
  - Increased risk of breast cancer
- Subsequent analysis of study with women starting HRT within 10 years of menopause (age 50-59)
  - No increased risk of heart disease (trend toward reduction)
    - Placebo group: increased risk
  - Synthetic estrogen alone: no increased risk of stroke or breast cancer
  - Lower risk of death from any cause

**Results from another study…**

- E3N cohort study – Fournier 2007
- 80,377 postmenopausal women
- E2 + Progesterone group
  - No increase or decrease in breast cancer
- E2 + MPA
  - 69% relative increase in risk of breast cancer

**Progesterone**

- Progesterone ≠ Progestin
  - MPA brings progesterone level to ZERO
- Production mainly relies on a cycle
  - Primarily found in the last 2 weeks of cycle
- Has receptor sites all over the body!
  - Brain, uterus, fallopian tubes, testicles, breast, vagina, adrenal glands, blood vessels, peripheral nerves, skin, eyes
- Moderates effects of excess estrogen
  - Reduces bloating, headache, bleeding, fibroids
- Important hormone in pregnancy

**Progesterone Benefits**

- Metabolizes out of the body quickly
- Improves sleep
- Natural calming effect
- Lowers high blood pressure
- Helps body use and eliminate fats
- Lowers cholesterol
- Neuroprotective
- Natural diuretic
- Anti-inflammatory
- Improves bone density

**Estrogen**

- Primarily secreted by ovaries
- Has 400 functions in the body!
- Primary hormone for the first 2 weeks of cycle
- 3 primary estrogens
  - Estriol (E3) = ~80% WEAK
  - Estradiol (E2) = ~10-20% STRONG
  - Estrone (E1) = ~5-10%
- Balance of estrogens changes as women age
  - Less estriol, more relative estradiol and estrone
- Estrogen metabolism is important

**Estrogen benefits**

- Offers cardiovascular protection
- May help prevent Alzheimer’s
- Increases metabolic rate
- Decreases LDL and prevents its oxidation
- Helps maintain memory
- Decreases wrinkles
- Maintains bone density
- Improves insulin sensitivity
- Regulates body temperature
- Increases sexual interest
- Prevents vaginal atrophy
- Helps urinary incontinence
Female Menstrual Cycle

Testosterone

YES, females need this too!!
- Secreted by ovaries and adrenal glands
- May convert to estrogen via aromatase enzyme
  - Aromatase enzyme predominantly found in fat cells
- Polycystic ovarian syndrome (PCOS) is associated with increased levels of testosterone

Testosterone benefits
- Increases libido
- Increases emotional sense of well-being
- Increases muscle mass and strength
- Helps maintain memory
- Helps skin from sagging
- Helps maintain bone strength
- Clitoral sensitivity

DHEA

- Dehydroepiandrosterone: Mother of all hormones
- Secreted primarily by the adrenal glands
- Maintains balance between anabolic and catabolic states
  - Maintains tissue strength and repair
  - Enhances immune system function

DHEA benefits
- Improves insulin sensitivity
- Promotes pain relief and relaxation
- Prevents plaque formation in arteries
- Decreases platelet aggregation
- Protects the brain
- Improves energy and memory
- Improves mood and well-being

Assessment

- Compounding or manufacturing?
  - Compounded Bi-Estrogen cream for a patient
  - Compounded pilocarpine lollipops for a dental office to be sold to their patients
- Which USP chapter pertains to non-sterile and which to sterile?
- Please identify these tools... (show)
- Which of the following is true of hormone replacement?
  - BHRT is structurally different and not recognized by the human body
  - BHRT copies nature and may provide a well-balanced therapy to maintain longevity and quality of life
  - The Women’s Health Initiative proves all hormones are evil
Assessment

True or False?

- Testosterone is not necessary for females; it turns them into werewolves!
- Estrogens cause breast cancer
- Osteoporosis gets more severe with hormone replacement
- Progesterone = Progestin
- There is a role for BHRT in treating women suffering from hormonal imbalances throughout their lives