Hot Topics in Compounded Medication 2023

Bryan Ziegler, PharmD, MBA

Clinical Compounding Pharmacist & Hormone Therapy Specialist

Moss Compounding Pharmacy

October 12, 2023, at 5:30 pm

Francis Marion University , Chapman Auditorium

List of Topics to Cover

- General information about compounded medication
- Hot Topics/Compounds of interest
  - Oral/Magic Mouth wash
  - Rectal preparations – hemorrhoids and fissures
  - Hormone Therapy
  - Low Dose Naltrexone (LDN)
  - Peptides
  - Dermatology/Anti-aging

What is a Compounding Pharmacy?

- A compounding pharmacy prepares personalized prescription medications for patients when a prescriber determines there's a medical need and manufactured drugs are not appropriate or available.
- Compound medications are "made from scratch," meaning individual ingredients are mixed together in the exact strength and dosage form required by each patient as directed by a prescriber. This allows a compounding pharmacist to work with patients and prescribers to customize medicines that meet a patient's specific needs.

Why use a compounding Pharmacy?

- Opens the door to a wide array of dosage form options
  - Delivering drugs in a different manner than commercially available
  - Great for patients with allergy issues
  - Ideal for dosing options that may not be available
- Allows for a more customized approach to medication treatment
  - The original “personalized medicine”
  - One size does not fit all approach
- Great options in times of drug shortage or discontinuation

Regulation of Compounding Pharmacy

- Board of Pharmacy
- FDA
- DEA
- DHEC
- EPA
- OSHA

What can be used in a Compound Medication

Requirements for Compounded Ingredients:
Under federal law (Section 503A), to be eligible for use in a compounded product, an active ingredient must meet one of the following criteria:

1. Be an active ingredient in an FDA-approved drug product.

2. Have a USP or National Formulary drug monograph.

3. Appear on the Section 503A Interim or Final Bulks List published by FDA.

Quality in Compounded Medications

- Ingredients –
  - Purchased from FDA registered suppliers
  - Evaluated to meet or exceed standards set by United States Pharmacopeia (USP) or National Formulary (NF)
- Compounding Process
  - Utilizing state of the art equipment along with traditional compounding techniques
  - Follow standards established by USP
- Quality testing
- Extensive documentation and record keeping

Not all compounding pharmacies are created equal….

- What's the scope of the compounding capability?
- What's the level of staff training/expertise?
- Does the pharmacy have the adequate equipment to make high quality preparations?
- How does the pharmacy ensure quality of the preparation?
- Does the pharmacy use quality ingredients in the preparations?
- Is the compounding pharmacy a valuable educational resource for prescribers?
- Does the pharmacist provide thorough education to patients on proper use?

Dosage forms

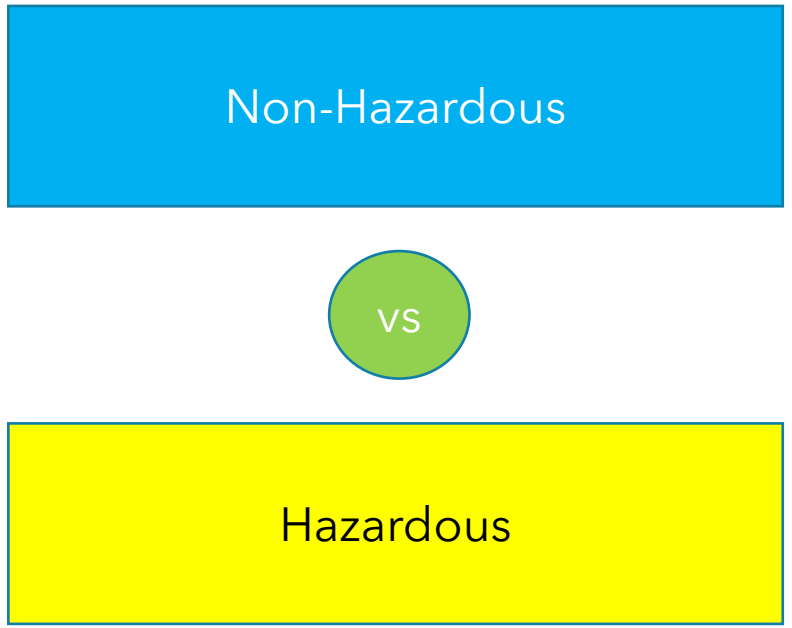
Dosage form categories for today's discussion

Non-sterile Dosage Forms

- Oral
- Topical
- Vaginal
- Rectal

Sterile Dosage Forms

- Injectables
- Ophthalmic preparations
- Nebulization products



Topical dosage forms

- Creams
- Gels
  - Hydrogel
  - Alcohol based
- Transdermal (permeation enhanced) gels*
- Ointments
- Lotions
- Shampoos
- Topical Solutions
- Otic drops/powders
- Deodorant
- Lip Balm
- Sprays
  - Topical
  - Nasal

What's **NOT** on the list:

- Transdermal patches

**Most Require specialized equipment*

***Requires specialized device*

Vaginal dosage forms

- Creams
- Ointments
  - mucoadhesive
- Gels
  - mucoadhesive
- Suppository
  - Fatty acid base
  - Cocoa butter base
  - Base A (PEG)

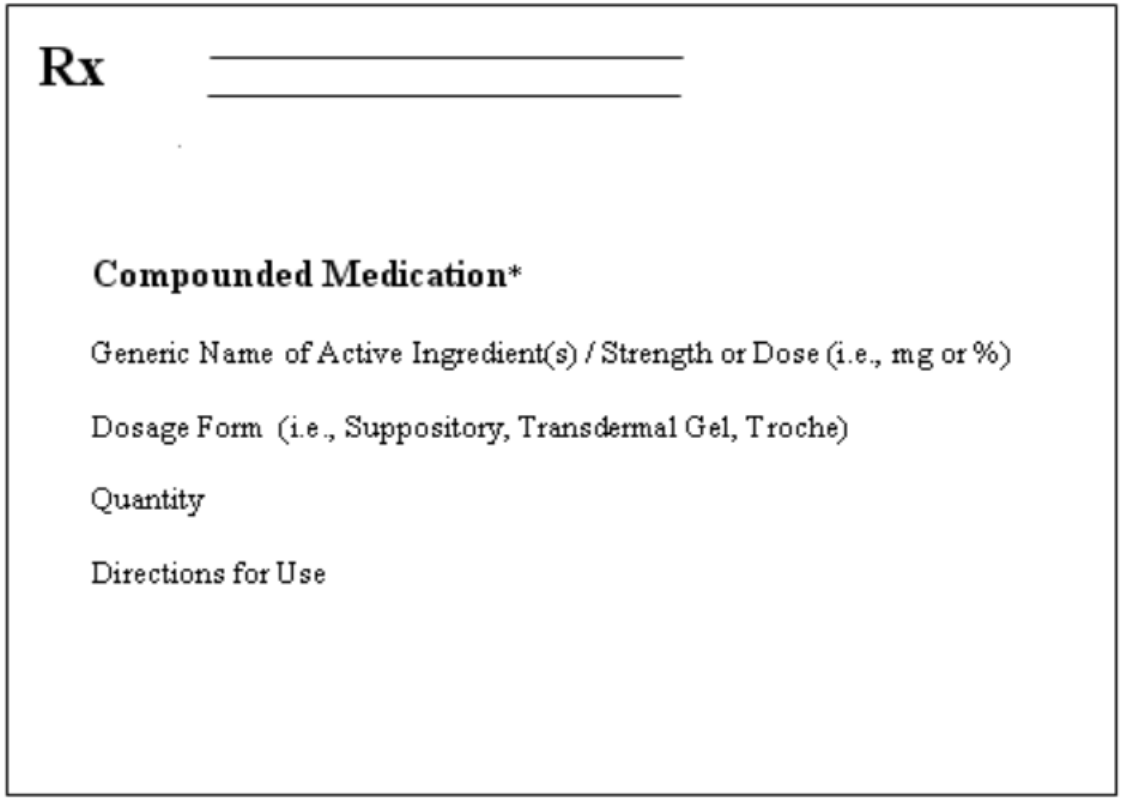
Rectal Dosage forms

- Gel
  - mucoadhesive
- Suppository
  - Base A (PEG)
  - Fatty Acid base
- Enema
- Ointment
- Cream

Sterile Dosage Forms

- Injectables
  - Aqueous Solutions
  - Oil based solutions
  - NOTE: Suspensions are typically considered difficult to properly compound and can results in inaccurate preparations with dosage variations or unstable final preparations.
- Ophthalmic preparations
  - Drops (solution)

Writing a Prescription for a Compounded Medication



*prescription should begin with the phrase "Compounded Medication"

Compound Examples

Magic mouthwash

Magic Mouthwash

- There's more than just 1 version
- Common uses:
  - Stomatitis
  - Mouth Irritation/ulceration
  - Thrush
  - Geographic tongue

Magic Mouthwash

- Currently we make over 80 versions of Magic Mouthwash
- Typical Ingredients:

Antibiotic:
Tetracycline or Doxycycline
Penicillin (alternative)

Anesthetic:
Lidocaine Viscous
Tetracaine

Anti-histamine:
Diphenhydramine Elixir
(Inflammation/Mild Anesthetic)

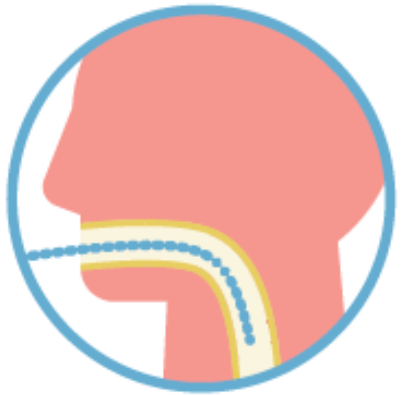
Anti-fungal:
Nystatin Suspension

Corticosteroid:
Hydrocortisone
Dexamethasone

Other:
Maalox/Mylanta
Kaopectate
Sucralfate
Misoprostol
Anti-virals

Magic Mouthwash – Other Considerations

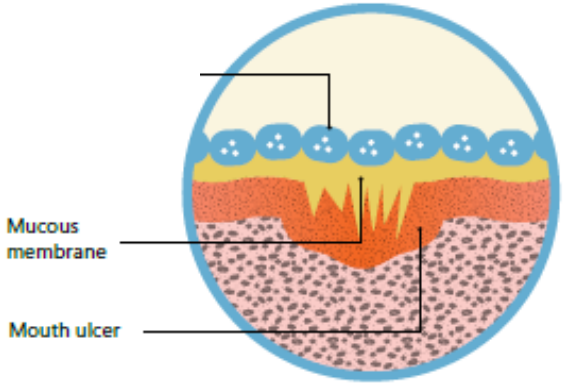
- Swish & Spit OR Swallow



Oral Application

Swish and spit for oral or swallow for esophageal.

- Viscosity & Muco-adhesion effect

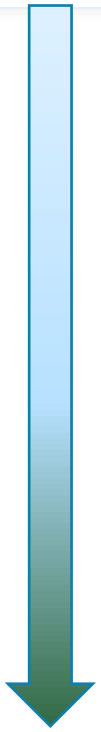


Stronger Adhesion

Bonds to mucousa to create a pwerful but lightweight coating effect.

Magic Mouthwash – Common Formulas

Thin



Thick

- Mary's Magic Mouthwash
  - 8oz: Hydrocortisone 30mg, Tetracycline 750mg, Nystatin Susp 30mL, Diphenhydramine Elixir QS to 240mL
- Duke's Magic Mouthwash
  - 8oz: Hydrocortisone 60mg, Nystatin Susp 60mL, Diphenhydramine Elixir QS to 240mL
- BMLN
  - 8oz: Diphenhydramine Elix, Maalox, Lidocaine Viscous, Nystatin Susp (1:1:1:1)
- BML (aka BMX)
  - 8oz: Diphenhydramine Elixir, Maalox, Lidocaine Viscous (1:1:1)
- Miles Magic Mouthwash
  - 8oz: Hydrocortisone 30mg, Tetracycline 750mg, Nystatin Susp 30mL, Diphenhydramine Elixir 60mL (QS to 240mL with cellulose based gel)

Rectal Preparations

Dosage forms we'll cover

- Suppositories
- Ointments/Creams
- Gels (Mucoadhesive)
- Enemas

Common conditions we're treating

- Hemorrhoids
- Fissures
- Proctitis
- Colitis

Suppositories

- Internal Options
  - For Hemorrhoids
  - Proctitis
  - Spasms

- Common Formulations:
  - Hydrocortisone 25mg/Pramoxine 10mg suppository
    - SIG: Insert 1 supp PR BID x 7-10 days
  - Prednisone suppository (5, 10, or 20mg options)
    - SIG: Insert 1 supp PR QHS x 7 days for proctitis
  - Diazepam 10mg (or 5mg) suppository
    - SIG: Insert 1 supp PR QD PRN rectal spasms

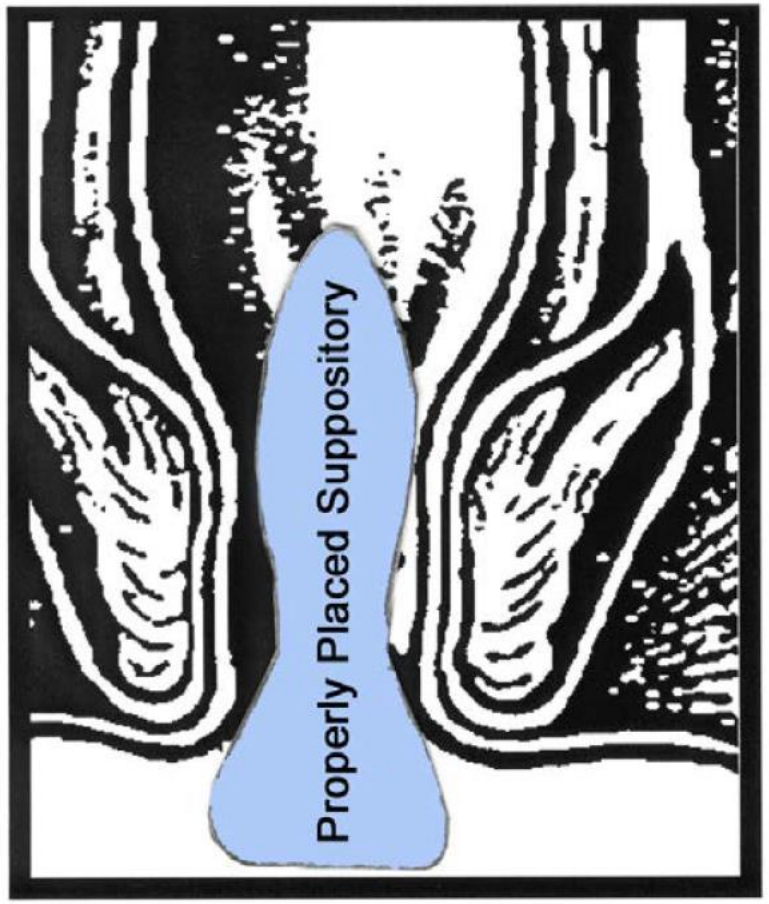
Suppositories

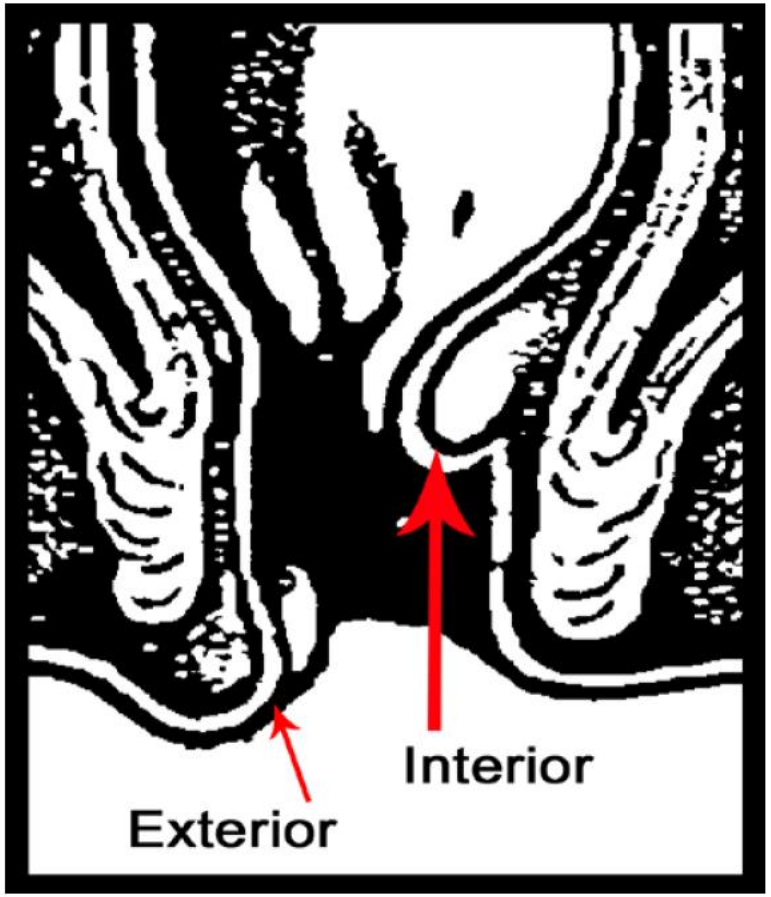
Rectal Rocket Suppository

- Unique shape allows for treatment of internal and external hemorrhoids simultaneously
- Typical formulation = Hydrocotisone 2.5%/Pramoxine 1%/ Lidocaine 2%
- SIG: 1 PR QHS x 3 nights (for mild to moderate cases)

Suppositories

- Rectal Rocket (continued)





Gel

Muco-adhesive Rectal Gel

- Great option for External hemorrhoids
- **Example Gel** (same formula as the suppository)
  - Hydrocortisone 2.5%/Pramoxine 1%/Lidocaine 2% Rectal Gel
  - SIG: Apply to affected area BID-TID x 7 days

Ointments/Creams

- Typical condition - Fissures
- Common formulations compounded:
  - Nitroglycerin 0.2% in Lanolin
  - Diltiazem 2% ointment
  - Nifedipine 0.2% ointment
  - Typical SIG (for all 3 above): Apply a “pea-size” amount BID
    - Application is peri-anal and/or to anal canal
    - NOTE: Nifedipine may be used up to QID

Ointments/Creams

- MOA:
  - Nifedipine/Diltiazem – relaxes internal anal sphincter by blocking calcium influx into sphincter smooth muscle cell cytoplasm, reducing spasms and facilitating healing
    - NOTE: muscle contractions can reduce blood flow to the anus and prevent the fissure from healing
  - Nitroglycerin - reduction in resting pressure of the internal anal sphincter, which decreases pain and further facilitates healing
    - Also dilates blood vessels and increases blood flow

Source: https://www.uptodate.com/contents/anal-fissure-beyond-the-basics. Accessed July 15, 2021

OINTMENTS/CREAMS

- Side Effects
  - NTG ointment - (more common with higher strength and applying too much)
    - Headaches - #1 reason for discontinuation
    - Lightheadedness upon standing
    - Mild burning/tingling sensation
    - Caution in patients with hypotension, utilizing erectile dysfunction meds
  - CCBs (Nifedipine/Diltiazem)
    - Less side effects compared to NTG
    - Caution with hypotension patients

- Several studies have indicated CCBs may be just as effective as NTG ointment, with treatment course lasting 2-6 weeks for most patients.
  - Use has been in acute and chronic fissures

Source: https://www.pharmacytimes.com/view/anal-fissures-a-real-pain July 2014;
Patel, Y et al. Treatment of Anal Fissure with Nifedipine/Lidocaine Ointment. *Am J Gastro*. Oct 2004

Potential Additions to Ointments/creams

- Lidocaine 1 – 5%
- Tetracaine 2-4%
- Misoprostol 6.67 mcg/gm

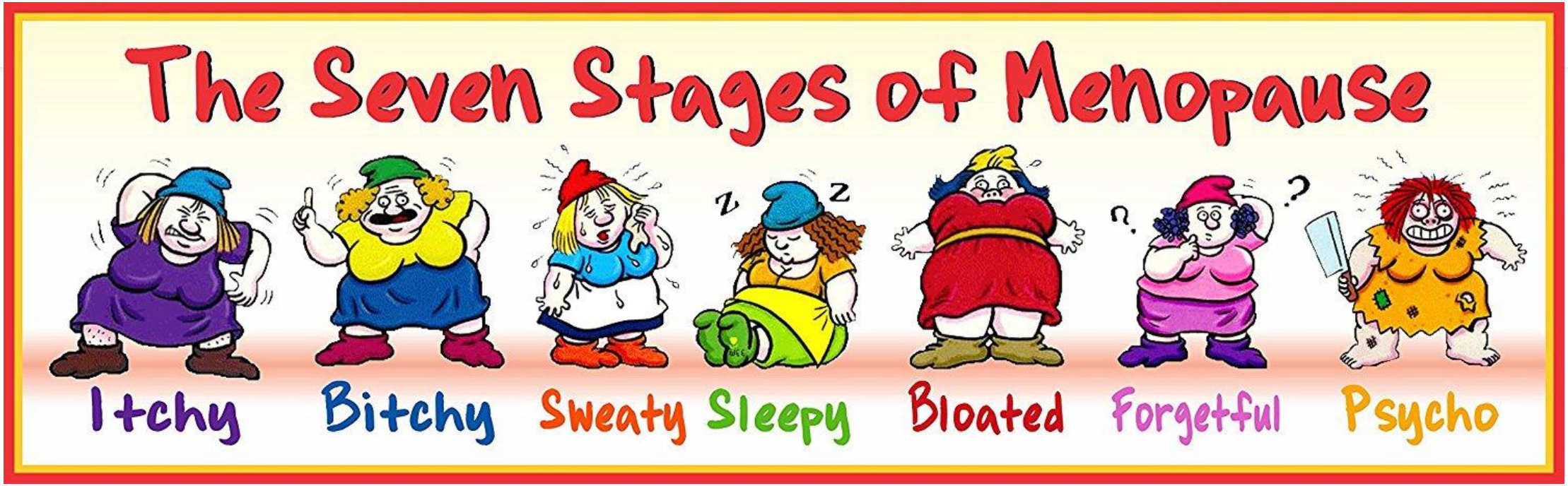
Hormone Replacement

Patient Populations

- Female
  - Pre-menopausal
  - High Risk Pregnancy
  - Peri-Menopausal
  - Menopausal
  - Post-Menopausal
- Male
  - Hypogonadism (“Andropause”)

Menopause: Symptoms

- Hot Flashes
- Hair loss
- Dry skin
- Sleep disturbances
- Night sweats
- Anxiety
- Vaginal Dryness
- Vaginal atrophy
- Irritability
- Memory loss
- Depression
- Nervousness
- Diminished sex drive
- Painful intercourse
- Urinary incontinence
- Heart palpitations


The Seven Stages of Menopause
Itchy
Bitchy
Sweaty
Sleepy
Bloated
Forgetful
Psycho

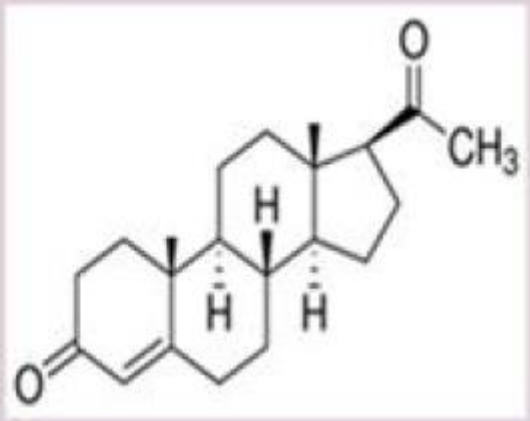
Symptom Relief Options

- Hormone Replacement Therapy (HRT)
  - Terms/Types
  - Risk/Benefit
    - What we know now
      - Estrogen - bio-identical options preferred, topical better than oral
      - Progesterone – bio-identical better results, different side effects
      - Testosterone – topical/sublingual/vaginal best ways to administer

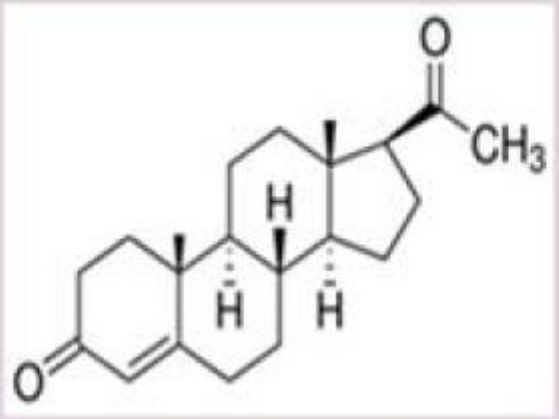
Terminology

- Bio-identical – same chemical formula on the molecular level as those found naturally in the human body
- Natural – derived from plant or animal source
- Synthetic – produced in a laboratory
- Progestin – synthetic hormone molecule that acts like progesterone in the body (mainly in the uterus)

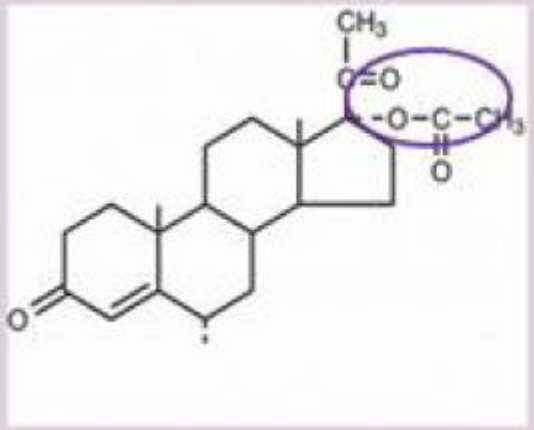
Chemical Structures Explain It All



Progesterone-Bioidentical

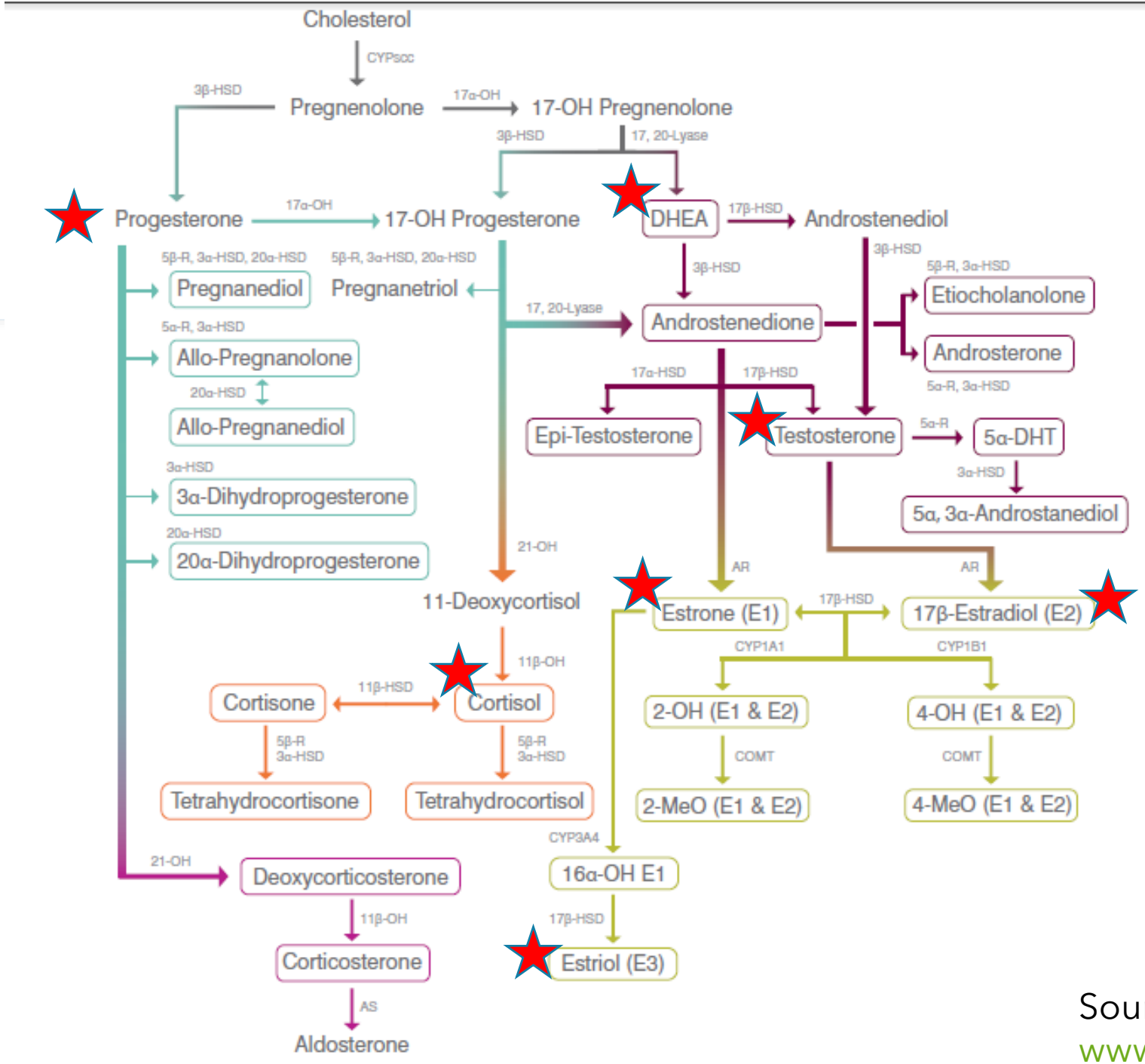


Physiological Progesterone

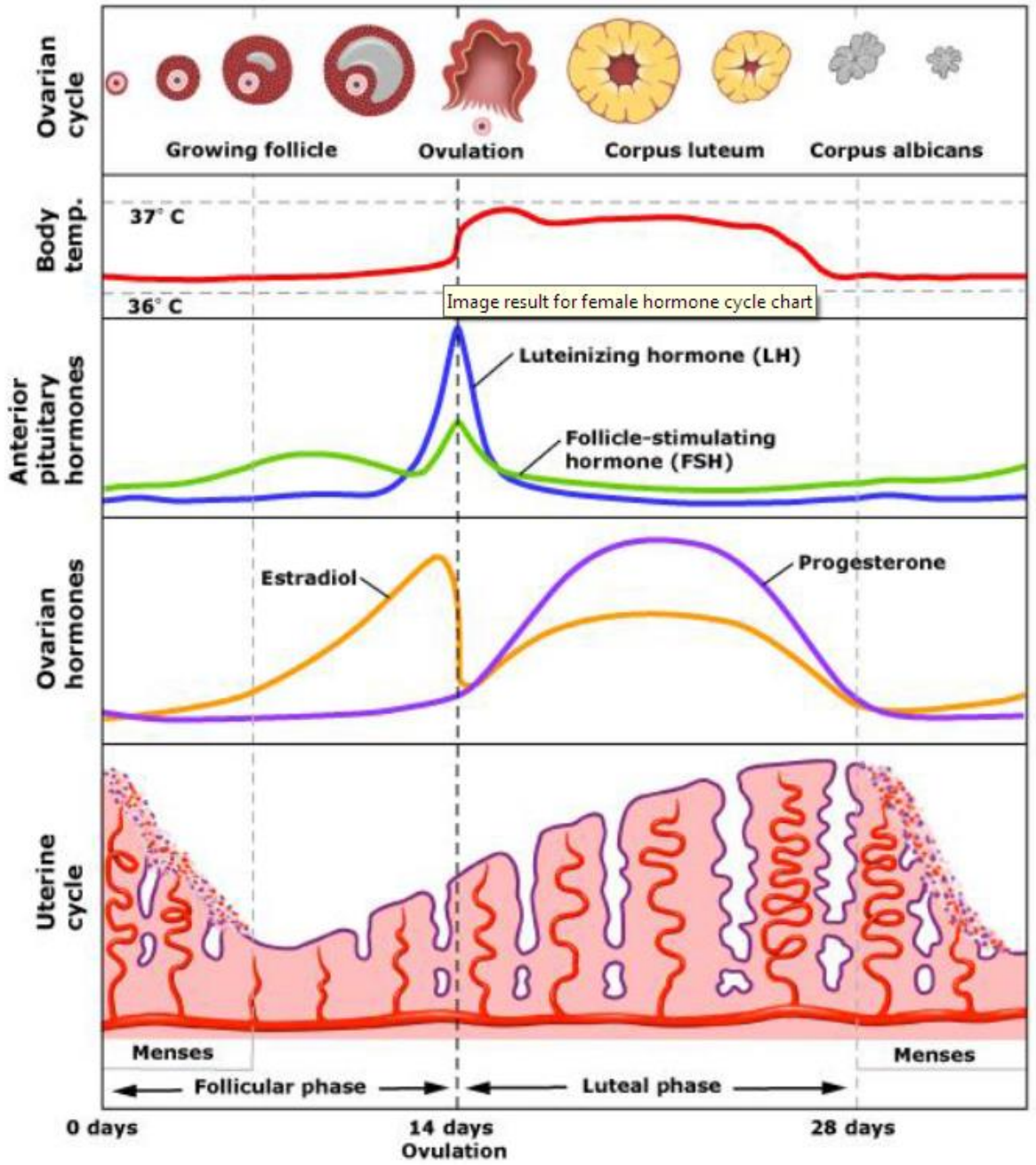


Medroxyprogesterone Acetate

<u>Bioidentical Hormone Therapy</u> are what many women are looking for when they say they want "natural hormone therapy".



Source:
www.zrtlabs.com


Ovarian cycle
Growing follicle
Ovulation
Corpus luteum
Corpus albicans
Body temp.
37° C
36° C
Image result for female hormone cycle chart
Anterior pituitary hormones
Luteinizing hormone (LH)
Follicle-stimulating hormone (FSH)
Ovarian hormones
Estradiol
Progesterone
Uterine cycle
Menses
Menses
Follicular phase
Luteal phase
0 days
14 days
Ovulation
28 days

Why use a Compounded HRT?

- Bio-identical ingredients
- Wide variety of dosage forms
- Individualized, Customizable dosage forms
  - Unlimited combinations/strengths available
  - Allows for improved compliance opportunities
- Avoid unwanted ingredients (allergies and/or adverse events)
  - Ex. Removal of propylene glycol with vaginal preps
  - Ex. Peanut allergy with commercial Micronized Progesterone

Unique Dosage forms - compounded HRT

- Creams
  - Topical
  - Vaginal
- Gels
- Ointments
- Capsules – IR, TR
- Troches
- Suppositories

What's Missing? - Pellets

Key Point – What Have I Learned….

- No two women are alike
  - Hormone levels fluctuating/changing
  - Symptoms are different
  - Other health conditions
  - Risk/Benefit
- Customization of therapy can be very beneficial to addressing symptoms and achieving desired results
- Thus….cookie-cutter approach to treatment typically doesn't produce the desired results.

Current Menopause HT Recommendations

- HT remains the most effective therapy for vasomotor symptoms and urogenital atrophy [1,2]

- Other menopause-related complaints, such as joint and muscle pain, mood swings, sleep disturbances, and sexual dysfunction (including reduced libido) may improve with HT. [1,2]

- Administration of **individualized** HT (including androgenic preparations when appropriate) may improve both sexuality and overall quality of life. [2]

1. NAMS Position Statement 2017. 2. International Menopause Society 2016

Current Menopause HT Recommendations

- HT should be part of an overall strategy including lifestyle recommendations regarding diet, exercise, smoking cessation, and safe levels of alcohol consumption.[1,2]

- HT **must be individualized and tailored** according to symptoms and the need for prevention, as well as personal and family history, results of relevant labs, and the woman's preferences & expectations. [1,2]

- Risk and benefits of HT differ for women during the menopause transition compared to those of older women. [1,2]

1. NAMS Position Statement 2017. 2. International Menopause Society 2016

Current Menopause HT Recommendations

- Dosage should be titrated to the **lowest effective dose**.[1,2]
- There are **no reasons to place mandatory limitations on duration** of HT. [1,2]
- Wide range of hormonal products and routes of administration, with potentially different risks and benefits. Thus, the term 'class effect' is confusing and inappropriate. However, evidence regarding differences in risks and benefits between products is limited. [2]

1. NAMS Position Statement 2017. 2. International Menopause Society 2016

Current Menopause HT Recommendations

- Spontaneous or iatrogenic menopause before age 45 (and particularly before age 40) = higher risk for CV disease & osteoporosis and possibly increased risk of dementia and affective disorders. HT may reduce symptoms and preserve bone density and is advised at least until the average age of menopause (51). [1,2]

- At least annual consultation including PE, updated medical & family Hx, relevant labs/imaging, recommended. Continue mammogram and pap smear on regular schedule. [1,2]

- Lower doses of HT may reduce symptoms and maintain QOL for women. However, long term data on lower doses regarding fracture or cancer risks and CV implications are still lacking. [2]

1. NAMS Position Statement 2017. 2. International Menopause Society 2016

Compounded Hormone Therapy

- *"…consider compounded HT if women cannot tolerate a government-approved therapy for reasons such as allergies to ingredients or for a dose or formulation not currently available in government-approved therapies."*

- North American Menopause Society

Position Statement 2017

(*Menopause*, Vol 24, No. 7, 2017)

FDA-APPROVED INDICATIONS

Vasomotor symptoms

Hormone therapy has been shown in double-blind RCTs to relieve hot flashes[23] and is approved as first-line therapy for relief of menopause symptoms in appropriate candidates.

Prevention of bone loss

Hormone therapy has been shown in double-blind RCTs to prevent bone loss, and in the WHI, to reduce fractures in postmenopausal women.[24,25]

Premature hypoestrogenism

Hormone therapy is approved for women with hypogonadism, POI, or premature surgical menopause without contraindications, with health benefits for menopause symptoms, prevention of bone loss, cognition and mood issues, and in observational studies, heart disease.[26-31]

Genitourinary symptoms

Hormone therapy has been shown in RCTs to effectively restore genitourinary tract anatomy, increase superficial vaginal cells, reduce vaginal pH, and treat symptoms of vulvovaginal atrophy (VVA).[32]

Key point

- Hormone therapy is approved by FDA for four indications: bothersome VMS; prevention of bone loss; hypoestrogenism caused by hypogonadism, castration, or POI; and genitourinary symptoms.

POI =Primary Ovary Insufficiency

Contraindications to Hormone Therapy

No absolute contraindications of hormone therapy have been established. However, HT is relatively contraindicated in certain clinical situations, such as patients with the following findings:

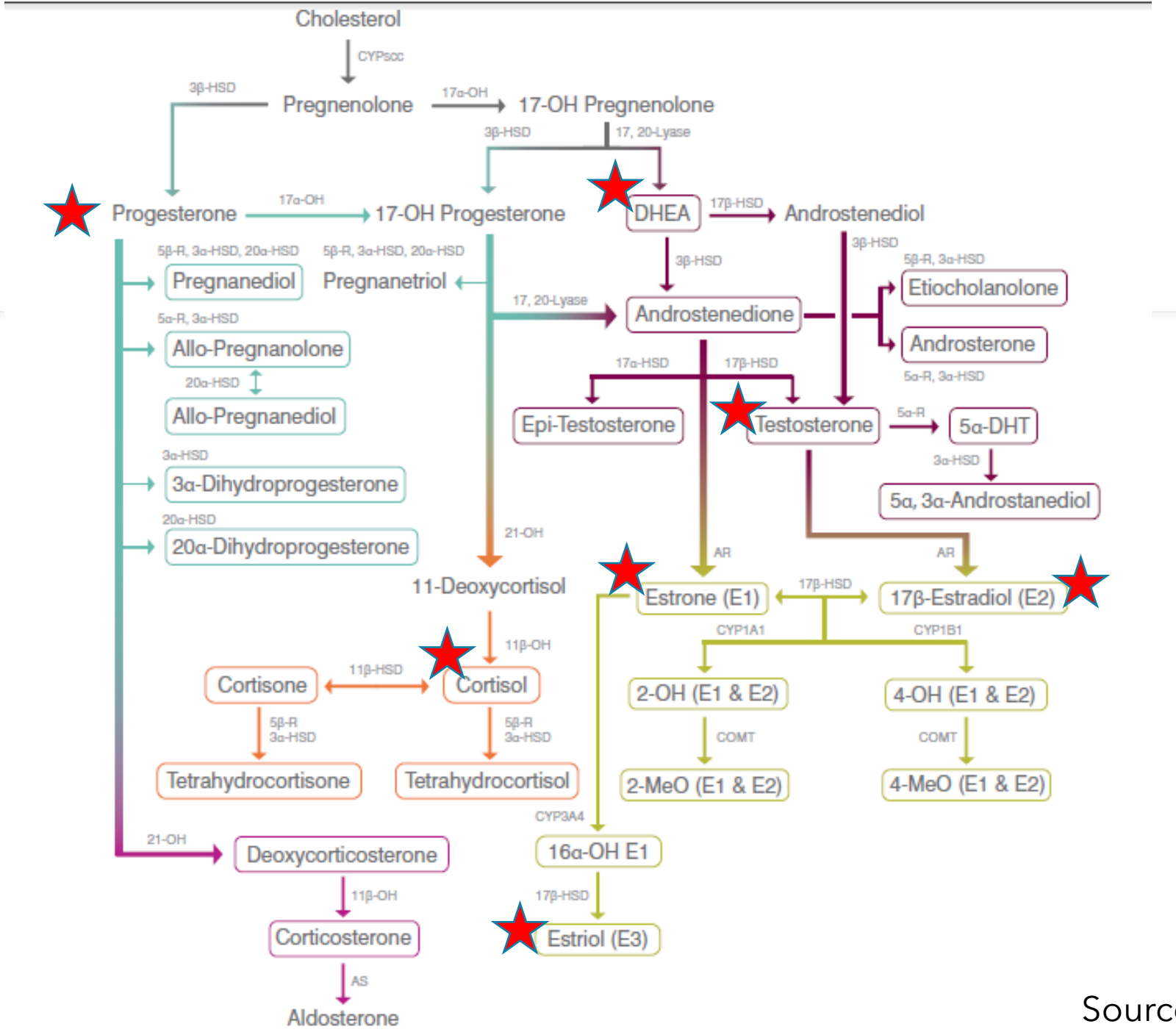
- A history of breast cancer
- A history of endometrial cancer (see Uterine Cancer and Endometrial Carcinoma)
- Porphyria
- Severe active liver disease
- Hypertriglyceridemia
- Thromboembolic disorders (see Deep Venous Thrombosis and Pulmonary Embolism)
- Undiagnosed vaginal bleeding (see Dysfunctional Uterine Bleeding)
- Endometriosis
- Fibroids

Note that many clinicians do not prescribe HT for women with a previous history of breast or endometrial cancer.

Kaur K, Lucidi R, et al. Menopause Hormone Replacement Therapy: Practice Essentials, Overview, Symptoms and Effects of Menopause. Medscape January 4, 2018. Accessed March 20, 2018.

How to Prescribe Compounded HRT

- Include the word “Compound” or “Compounded” on Rx
- Estrogen Component
  - Estriol (E3)
  - Estradiol (E2)
  - Estriol (E3) + Estradiol (E2) = Bi-estrogen
    - Indicate ratio of Bi-estrogen mix + strength + SIG
    - Ex. Bi-estrogen (80:20) 1mg topically QD
      - Ratio is (E3:E2), thus 80% E3 and 20% E2 in this compound
- Progesterone
  - Oral: “Compounded Progesterone”; TR or SR ___mg
- Testosterone
- DHEA
- ***Can be ordered as separate dosage forms or combined***



Source: www.zrtlabs.com

How to Prescribe Compounded HT

- Example of combined HRT compound Rx:

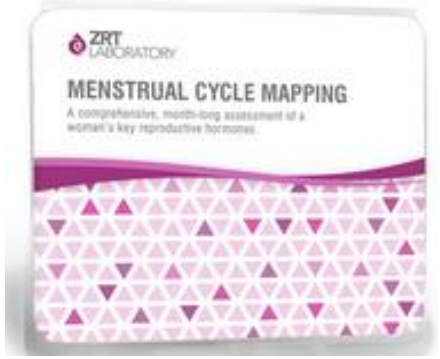
Bi-estrogen (80:20) 1mg
Progesterone 40mg
Testosterone 2mg
} per mL cream

Qty: QS for 1month

SIG: Apply 0.5mL topically or vaginally QD on days 1-25 of the month

Additional Role of Compounding Pharmacist (Specializing in HRT)

- Services
  - Hormone evaluations/consultations in collaboration with prescriber
  - Hormone therapy recommendations
  - Medication compounding
  - Hormone therapy monitoring
  - Saliva, Blood spot, urine testing



Key Point – What Have I Learned….

ELSE

- No two women are alike
  - Hormone levels fluctuating/changing
  - Symptoms are different
  - Other health conditions
  - Risk/Benefit
- Customization of therapy can be very beneficial to addressing symptoms and achieving desired results
- Thus….cookie-cutter approach to treatment typically doesn't produce the desired results.
- ***Clinically treating and managing hormone therapy patients takes time.***

Low Dose Naltrexone (LDN)

Low Dose Naltrexone (LDN)

- We are discussing NAL**TREX**ONE

Not Naloxone (for opioid reversal)

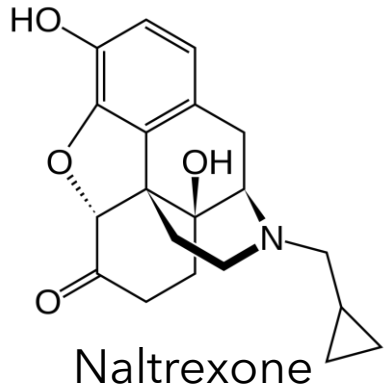
What is LDN?

- LDN is a competitive opioid receptor antagonist.
- At the standard “full strength” dose (50-100mg), naltrexone blocks the effects of both the endogenous opioids, which are in endorphins and pharmaceutical opioids.
- But today we are talking about **LOW DOSE** Naltrexone

What is LDN?

- LDN is a pure antagonist, therefore it is NOT a controlled substance, narcotic, or opioid.
- It is a pure antagonist at various opioid receptors, Delta Kappa, Mu, and Opioid Growth Factor (OGF) receptors.
- The chemical structure is almost identical to endorphins that we make naturally called met-enkephalin, also known as OGF or Opioid Growth Factor.

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn



Naltrexone

What is LDN?

- LDN is an antagonist at the OGF receptors and there are OGF receptors on a wide range of cells in the body.
- When we talk about low dose naltrexone (LDN) we mean doses that are a 10th or less of the standard dose of Naltrexone.
- Most of the research studies have used 4.5mg per day.
- Doses range from 0.001mg – 16mg in clinical practice.

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

What is LDN?

- “It reduces pain, and fights inflammation. It is used to treat cancers, autoimmune diseases, chronic pain and mental health issues, to name a few. Treatment is constantly evolving, with new conditions and methods of treatment being shared regularly.”

  - LDN Research Trust

    https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

LDN 2022 Dosing Information For Prescribers

Naltrexone dosing considerations:
"Ultra low dose" when given daily in microgram dosing – dosed twice daily
"Very low dose" when given in daily dose of less than 0.1-0.5 mg
"Low dose" when given in daily dose (or split doses) less than or equal than 4.5-10 mg
"Moderate dose" when the daily dose is between 10-25mg
"High dose" when given in daily amounts of 50mg or more

LDN (low-dose naltrexone) is compounded in various forms in the US. The LDN Research Trust works closely with compounding pharmacies and qualified pharmacists to prescribers and their patients. Fillers can vary from pharmacy to pharmacy but generally include microcrystalline cellulose, sucrose, or a probiotic – depending on a patient's individual

LDN 2022 Dosing Information

https://ldnresearchtrust.org/sites/default/files/2022-01/Dosing-Info-2021.pdf

History of naltrexone & LDN

- Naltrexone was synthesized in 1963 as an orally active competitive opioid receptor antagonist.
- Naltrexone is structurally and functionally similar to the opioid antagonist naloxone, but it has greater oral bioavailability and a longer biologic half-life.
- Naltrexone HCl was approved by FDA in 1984 for the treatment of opioid addiction. The typical daily dosage for opioid addiction is 50–100 mg daily, and 50-mg tablets are available commercially.
- The effects of LDN were first discovered in the late 1980s

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

Pharmacologic effects

- Low Dose Naltrexone binds to the endorphin receptors for about 1 – 1/2 hours, and the blockade lasts about 4 - 6 hours.

- The effects of LDN are analgesia and anti-inflammatory.

- One of the other effects is that it increases the production of endogenous endorphins.

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

Pharmacologic effects

- Naltrexone exists in a racemic mixture of isomers ("left-handedness and right-handedness")
- Dextro-naltrexone binds toll-like receptors (TLR)
- Levo-naltrexone binds opioid receptors

Levo-naltrexone

- Antagonist effect at opioid receptors
- Small temporary opioid blockade
- Upregulates endogenous opioid production
- Upregulates opioid receptors
- Increased endorphins favorable to the immune system

Dextro-naltrexone

- Antagonist effect at Toll-like receptors (TLR)
- TLR-4 receptors exist on microglial cells, other macrophages, mast cells
- Activated microglial cells produce proinflammatory cytokines, substance P, nitric oxide
- Inhibition leads to a decreased proinflammatory cascade

Modulate Immune response via Increase Endorphins

Anti-inflammatory & Suppressed Cytokine modulated immune response (modulation)

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

Pharmacologic effects

- Endorphins are your natural peptides produced in many cells which regulate cell growth, including your immune cells. **Many patients who have autoimmune disease tend to have low levels of endorphins, Met-enkephalin**, aka opioid growth factor (OGF), an important immunomodulator.
- Opioid receptors are in the central and the peripheral nervous system, the GI tract, and on lymphocytes.
- By using **LDN you receive a brief blockade, creating a rebound effect giving you more endorphins, including OGF, and increased production of the OGF receptors**.

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

Important note

- Taking Naltrexone in larger doses of 50-300mg seems to **negate the immunomodulatory effect by overwhelming the receptors**, so **for the effect to work, the dose must be in the range of 0.5-10mg, usually maxing at 4.5mg in clinical experience**.

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

Side Effects

- Many patients who start LDN do not experience any severe side effects.
- Most common SE:
  - Vivid Dreams/Sleep disturbances (likely due to increase in endorphin release)
  - Headache
  - Anxiety
- In <10% of cases treated, increased introductory symptoms may be more severe or more prolonged than usual, lasting sometimes for several weeks. Rarely, symptoms may persist for two or three months before the appropriate beneficial response is achieved.
- Some patients very rarely experience gastrointestinal side effects, such as nausea and or constipation/diarrhea.
  - Reason for this is currently unknown, but may be due to the presence of large numbers of delta-opiate receptors in the intestines.

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

Published in final edited form as:
Pain Med. 2009 ; 10(4): 663–672. doi:10.1111/j.1526-4637.2009.00613.x.

Fibromyalgia Symptoms Are Reduced by Low-Dose Naltrexone: A Pilot Study

Jarred Younger, PhD and **Sean Mackey, MD, PhD**
School of Medicine, Department of Anesthesia, Division of Pain Management, Stanford University, Palo Alto, California, USA

Abstract

Objective—Fibromyalgia is a chronic pain disorder that is characterized by diffuse musculoskeletal pain and sensitivity to mechanical stimulation. In this pilot clinical trial, we tested the effectiveness of low-dose naltrexone in treating the symptoms of fibromyalgia.

Design—Participants completed a single-blind, crossover trial with the following time line: baseline (2 weeks), placebo (2 weeks), drug (8 weeks), and washout (2 weeks).

Patients—Ten women meeting criteria for fibromyalgia and not taking an opioid medication.

Interventions—Naltrexone, in addition to antagonizing opioid receptors on neurons, also inhibits microglia activity in the central nervous system. At low doses (4.5 mg), naltrexone may inhibit the activity of microglia and reverse central and peripheral inflammation.

Outcome Measures—Participants completed reports of symptom severity everyday, using a handheld computer. In addition, participants visited the lab every 2 weeks for tests of mechanical, heat, and cold pain sensitivity.

Results—Low-dose naltrexone reduced fibromyalgia symptoms in the entire cohort, with a greater than 30% reduction of symptoms over placebo. In addition, laboratory visits showed that mechanical and heat pain thresholds were improved by the drug. Side effects (including insomnia and vivid dreams) were rare, and described as minor and transient. Baseline erythrocyte sedimentation rate predicted over 80% of the variance in drug response. Individuals with higher sedimentation rates (indicating general inflammatory processes) had the greatest reduction of symptoms in response to low-dose naltrexone.

Conclusions—We conclude that low-dose naltrexone may be an effective, highly tolerable, and inexpensive treatment for fibromyalgia.

Clin Rheumatol. 2014; 33(4): 451–459.
Published online 2014 Feb 15. doi: 10.1007/s10067-014-2517-2
PMCID: PMC3962576
PMID: 24526250

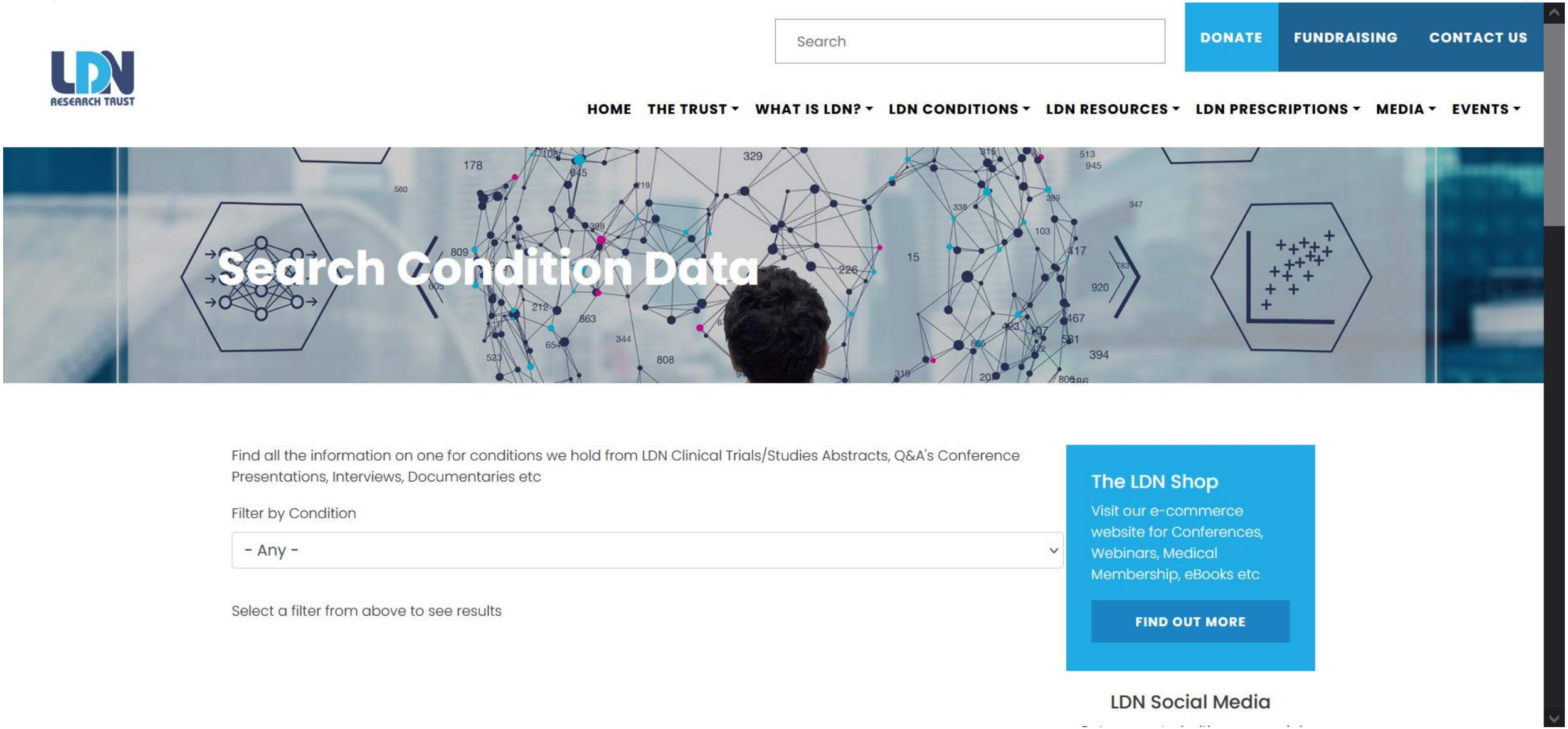
The use of low-dose naltrexone (LDN) as a novel anti-inflammatory treatment for chronic pain

Jarred Younger,[1,4] Luke Parkitny,[2] and David McLain[3]

Abstract

Go to: ▸

Low-dose naltrexone (LDN) has been demonstrated to reduce symptom severity in conditions such as fibromyalgia, Crohn's disease, multiple sclerosis, and complex regional pain syndrome. We review the evidence that LDN may operate as a novel anti-inflammatory agent in the central nervous system, via action on microglial cells. These effects may be unique to low dosages of naltrexone and appear to be entirely independent from naltrexone's better-known activity on opioid receptors. As a daily oral therapy, LDN is inexpensive and well-tolerated. Despite initial promise of efficacy, the use of LDN for chronic disorders is still highly experimental. Published trials have low sample sizes, and few replications have been performed. We cover the typical usage of LDN in clinical trials, caveats to using the medication, and recommendations for future research and clinical work. LDN may represent one of the first *glial cell modulators* to be used for the management of chronic pain



https://ldnresearchtrust.org/search-condition

Our Current Experience

- Have been treating patients for over 4 years with LDN
- Currently have an active treatment population of 127 patients
  - Most common diagnoses treating:
    - Fibromyalgia
    - Rheumatoid Arthritis
    - Chronic pain
    - IBS/Crohn's/Colitis
    - Lupus
    - MS
  - 76% currently on therapy and reporting symptom improvement
  - 24% discontinue or loss to follow up
    - Limited response during titration phase/unrealistic expectations
    - Side effects

Case reports

- ER is a 75 yo female who presented with chronic pain and fibromyalgia
- Previous meds
  - Opiate (Oxycodone/APAP) PRN (wanted to d/c)
  - Pregabalin
  - Milnacipran (tried and d/c)
- Started on LDN
  - D/c opiate, Pregabalin
  - Within 4 weeks reported tremendous pain improvement (pain scale score dropped from 8 to 2) and improved QOL
  - Current dose = 6mg po QD (target was 4.5mg)

Case reports

- JA is 51 yo male who presented with severe colitis
- Patient reported at LDN therapy initiation that:
  - Condition was chronic
  - Had tried all the standards of therapy with limited results
  - Was afraid to go too far away from home/restroom
  - High level of gastrointestinal discomfort
- Started LDN (target dose was 3mg – 4.5mg)
  - Started low, increased dose slowly
  - Patient reported some initial loose stool which subsided. Also reported this when attempting to increase dose above 2mg.
  - Patient currently at 2mg po QHS
  - Reports tremendous improvement in symptoms and glowing feedback on therapy. "Wish I started this med sooner"

Peptides

Peptides

Requirements for Compounded Ingredients:
Under federal law (Section 503A), to be eligible for use in a compounded product, an active ingredient must meet one of the following criteria:

1. Be an active ingredient in an FDA-approved drug product.

2. Have a USP or National Formulary drug monograph.

3. Appear on the Section 503A Interim or Final Bulks List published by FDA.

Additionally, peptides must not be classified as a biologic (defined as greater than 40 amino acids) in order to be compounded in a traditional compounding pharmacy.

Semaglutide / Tirzepatide

- Glucagon-like peptide-1 (GLP-1) receptor agonists stimulate insulin secretion and inhibit glucagon release in a glucose-dependent manner, which improves glycemic control with a low risk of hypoglycemia.
- Unlike many other therapies for type 2 diabetes mellitus, GLP-1 receptor agonists have been shown to also reduce body weight

https://accp1.onlinelibrary.wiley.com/doi/full/10.1002/cpdd.938 Accessed 8/1/23

Semaglutide

- protein- and peptide-based drugs like GLP-1 analogues, degradation in the stomach because of low pH and proteolytic enzymes is a major barrier to achieving sufficiently high systemic bioavailability after oral administration. Furthermore, absorption of proteins and peptides is compromised by the limited permeability through the gastrointestinal epithelium
- an oral tablet formulation of semaglutide has been developed by coformulation with the absorption enhancer sodium N-(8-[2-hydroxybenzoyl] amino) caprylate (SNAC).
  - SNAC is thought to protect against proteolytic degradation of semaglutide through a localized increase in pH and to facilitate the absorption of semaglutide across the gastric epithelium primarily via the transcellular route

https://accp1.onlinelibrary.wiley.com/doi/full/10.1002/cpdd.938 Accessed 8/1/23

Semaglutide

- Must be the base form and not salt form (bullet #1 prev slide)
- Injection form can be compounded as long as commercial products are on FDA shortage list
- Other dosage forms
  - Oral/Sublingual – requires SNAC (does SL need it???)
  - Nasal spray

https://reference.medscape.com/drug/ozempic-rybelsus-wegovy-semaglutide-1000174 Accessed 8/1/23

GLP-1 Agonists Linked to Higher Risk for Rare but Serious GI Complications

Damian McNamara, MA
October 05, 2023

People taking semaglutide or liraglutide for weight management are at a higher risk for rare but potentially serious gastrointestinal issues, compared with those taking naltrexone/bupropion, according to a large epidemiologic study.

Patients taking either of these glucagon-like peptide-1 (GLP-1) receptor agonists had nine times an elevated risk for pancreatitis. They were also four times more likely to develop bowel obstruction and over 3.5 times more likely to experience gastroparesis.

The research letter was published online today in *Journal of the American Medical Association*.

Investigators say their findings are not about scaring people off the weight loss drugs, but instead about increasing awareness that these potential adverse outcomes can happen.

"Given the wide use of these drugs, these adverse events, although rare, must

https://www.medscape.com/viewarticle/997128?ecd=WNL_mdpls_231010_mscpedit_pharm_etid5939443&uac=46277BZ&spon=30&impID=5939443 Accessed 10/11/23

Dermatology/Anti-aging

Topical Anesthetic

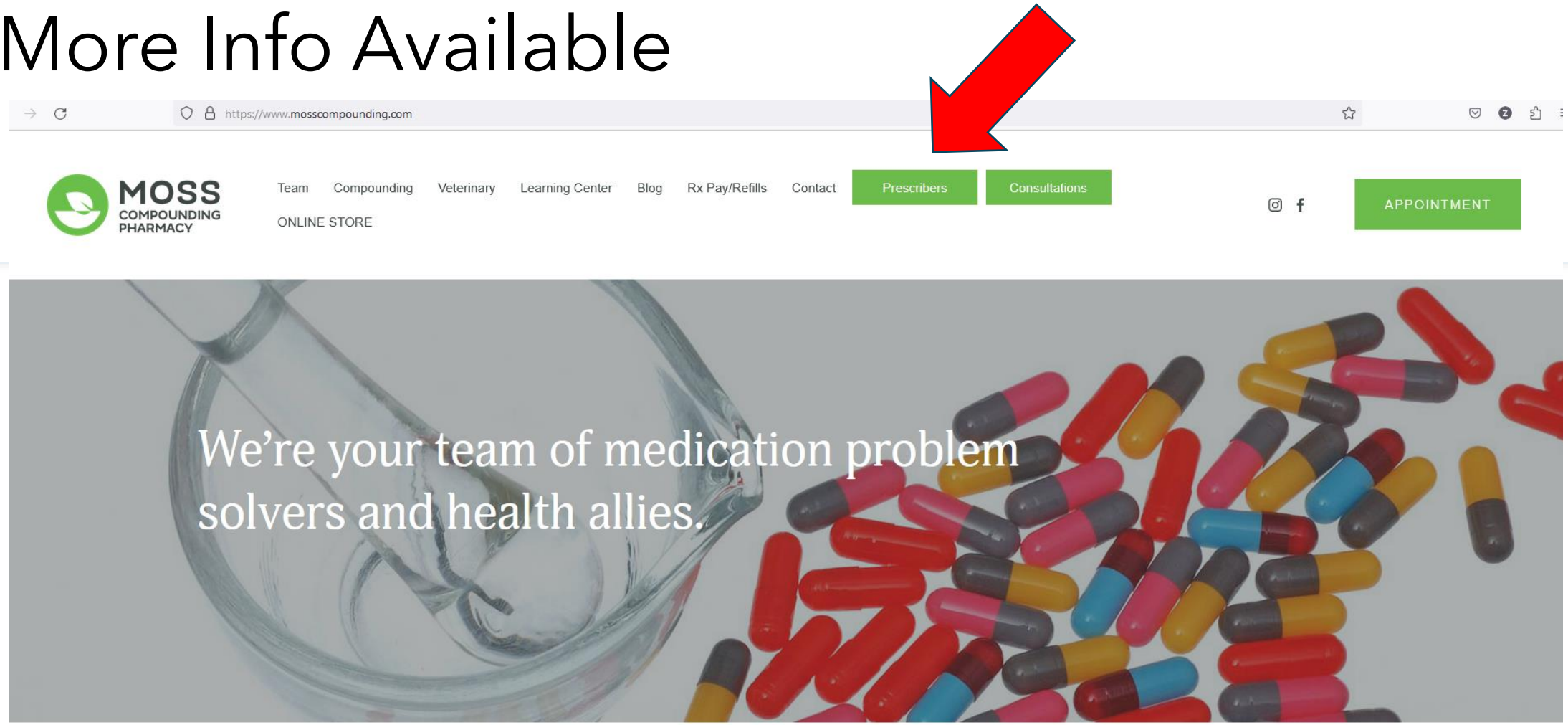
- Common Formulations include: (in various strengths)
  - Benzocaine
  - Lidocaine
  - Tetracaine

- Multiple base options
  - Plasticized Ointment
  - Petrolatum
  - Emollient Cream
  - Permeation Enhanced gel

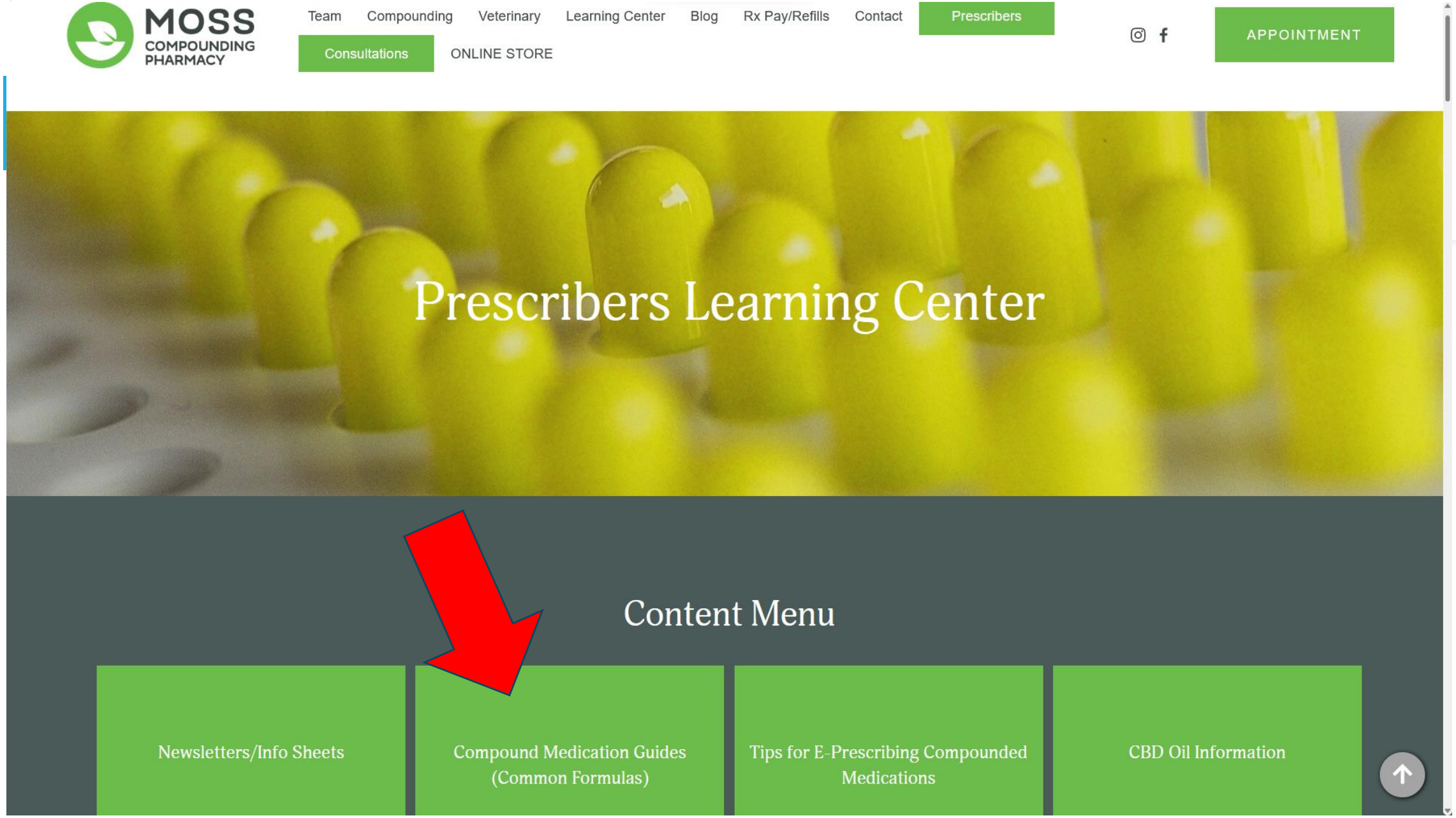
Anti-aging Formulations

- Common Ingredients Options:
  - Hydroquinone 2-8%
  - Kojic Acid 2-4%
  - Tretinoin 0.025-0.1%
  - Estriol 0.2%
  - Lactic Acid 2.5%
  - Glycolic Acid 2.5%
  - Salicylic acid 2%
  - Ascorbic Acid (Vit C)

More Info Available



We're not your typical pharmacy.


MOSS
COMPOUNDING
PHARMACY
Team
Compounding
Veterinary
Learning Center
Blog
Rx Pay/Refills
Contact
Prescribers
Consultations
ONLINE STORE
APPOINTMENT
Prescribers Learning Center
Content Menu
Newsletters/Info Sheets
Compound Medication Guides (Common Formulas)
Tips for E-Prescribing Compounded Medications
CBD Oil Information

Speaker Contact Information

Bryan Ziegler, PharmD, MBA

Moss Compounding Pharmacy

2500 Hoffmeyer Road, Florence, SC 29501
Email - bziegler@mosscompounding.com
Office Phone: 843.665.0289

www.mosscompounding.com

Questions?