Practical Contraception Review: OCP and EC

So many choices, where to start, and where to go

Alora Simpson, PharmD Intern 2023
Marina Rountree-James MD CCFP

Presenters

- Alora Simpson PharmD Intern
  - PharmD Intern graduating in 2023 from U of M
  - Experience in community, long-term care, hospital and primary care pharmacy settings
  - No conflicts of interest
- Marina Rountree-James MD CCFP (she/her)
  - Completed med school at UM 2017 and family med residency in the Winnipeg Urban stream 2019
  - Work at Access Fort Garry and Women's Health Clinic
  - No conflicts of interest

FOR CLARITY WE MAY USE TRADE NAMES AS WELL AS GENERIC

Learning Objectives

- Discuss hormonal contraception – combined oral contraceptives (COCs) and emergency contraception
- Understand the components of COCs
- Understand the different dosing options and formulations of COCs
- Understand how one would select a COC
- Identify the signs of hormone deficiency and hormone excess
- Understand how to change amongst COCs

Menstrual cycle

Normal frequency q 24-38d

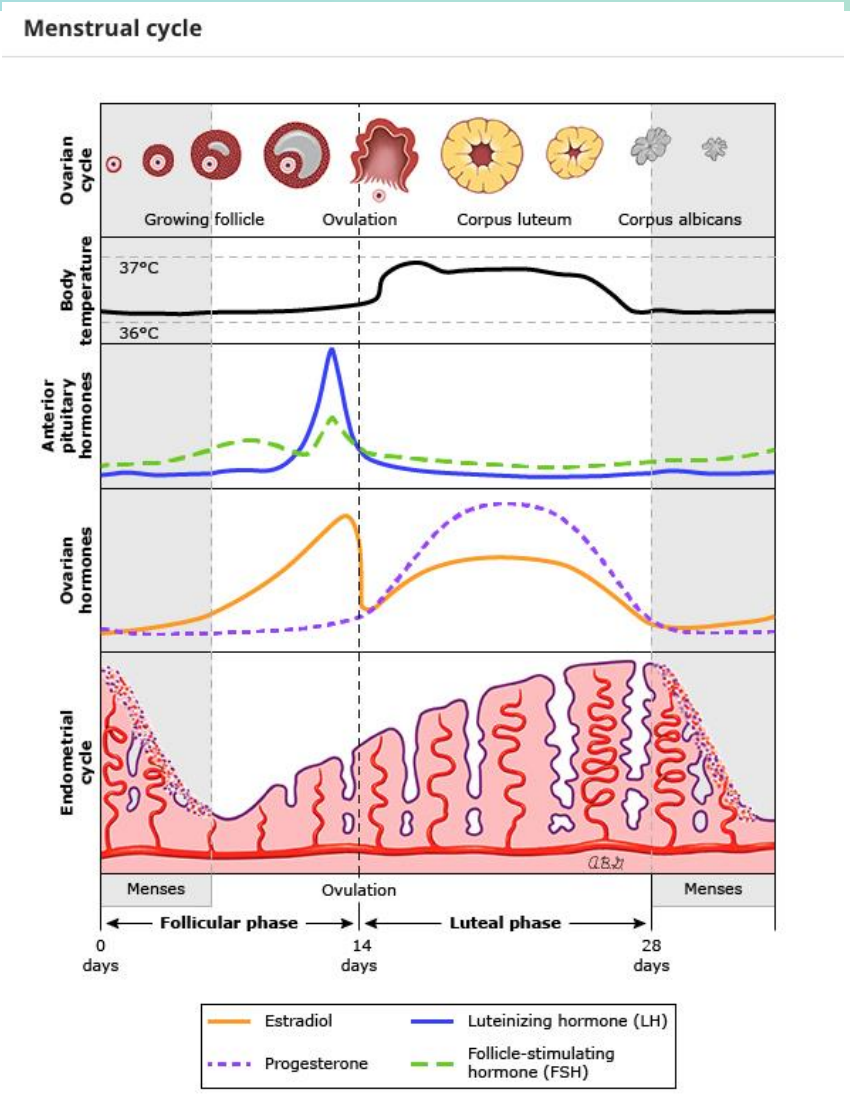
Bleeding normally equal or less than 8d

Follicular phase – onset of menses, ends day before luteinizing hormone (LH) surge

- Estrogen predominant

Luteal phase – begins day of LH surge, ends at onset of next menses

- Progesterone predominant



Graphic 62189 Version 4.0

Hormonal contraception

Estrogen:

- Increases the synthesis of estrogen and progesterone receptors
- Suppresses FSH release
- Prevents follicular maturation

Progesterone:

- Decreases synthesis of receptors and responsiveness to estrogen and progesterone
- Suppresses LH surge, preventing ovulation
- Reduces endometrial development

Table 2 Percentage of women experiencing unintended pregnancy within the first year of perfect and typical use, percentage of women continuing use at the end of the first year, and percentage of sexually active Canadian women using contraceptives

Adapted from Table 3-2 in Contraceptive Technology 2011, 20th edition,[31] with data from Black et al.[17]

Tier of effectiveness	Contraceptive method	% of women experiencing a pregnancy within the first year of perfect use	% of women experiencing a pregnancy within the first year of typical use	% of women still using the method at the end of one year	% of sexually active Canadian women who are not trying to conceive using each method[17]
I	IUC progesterone-releasing (IUS)	0.2	0.2	80	2
I	IUC copper-releasing (IUD)	0.6	0.8	78	2.3
I	Implant(Implanon)	0.05	0.05	84	0.1
I	Vasectomy	0.5	0.5	100	7.4
I	Tubal ligation	0.1	0.15	100	6.0
II	Progest(Depo-Perone injection rovera)	0.2	6	56	2.4
II	Combin(pill, pated hormonal contraceptive ch or ring)	0.3	9	67	45.5
III	Diaphragm	6	12	57	0.2
III	Male condom	2	18	43	54.3
III	Female condom	5	21	41	0.3
III	Sponge,spermicide	9–20	12–28	36–42	0.8
III	Coitus interruptus ("withdrawal")	4	22	46	11.6
III	Natural family planning No method	0.4–5 85	24 85	47	2.5 14.9*

Figures add to more than 100% because some women used more than one method.

IUC: intrauterine contraceptive

*** Different denominator from other figures in this column.**

Canadian contraceptive consensus Ch 1, https://www.jogc.com/action/showFullTableHTML?isHtml=true&tableId=t0005&pii=S1701-2163%2816%2939370-7; viewed 30 Nov 2022

Combined Oral Contraceptives (COCs)

How to know which one is the right one

Alora Simpson, PharmD Intern 2023

What is in a COC anyways?

Estrogen

Almost always ethinyl estradiol

Estrogen doses

High dose: ≥50 mcg	Low dose: 20-35 mcg	Ultra-low dose: <20mcg

Progestin

- The generations
  - 1st: Norethindrone
  - 2nd: Levonorgestrol
  - 3rd: Desogestrel
  - 4th: Drosiprenone

Progestin Generations

1st generation

4th generation

The generations refer to when the progestin group was introduced to market, however, 3rd and 4th generation progestins tend to be less androgenic and may have fewer side effects

The 4th generation progestin, Drosiprenone, may slightly increase VTE risk, in addition to the estrogen component

Estrogen Doses

High Dose

- Discontinued due to
  - High frequency of adverse events
  - Risk of venous thromboembolism

Low Dose/Ultra-Low Dose

- Significantly improved safety compared to high dose
- Ultra-low dose may not further reduce adverse events

New Estrogen

Estradiol

- Synthetic estrogen
- Fully agonistic
- VTE risk
- On formulary

Estetrol

- Natural estrogen
- Mixed antagonistic and agonistic activity (less impact on breast and liver)
- VTE risk
- Not on formulary

Common Side Effects

- Nausea/Vomiting
- Bloating
- Headache
- Breakthrough bleeding*
- Breast tenderness
- Typically resolve within 3 months of use

Types of Bleeding

- Breakthrough bleeding: Bleeding that occurs while taking active pills ie. during weeks 1-3

- Withdrawal bleeding: Scheduled bleeding that occurs during the hormone free interval

Warning Signs with COC Use (ACHES)

- A: abdominal pain (severe)
- C: chest pain (sharp, crushing)
- H: headaches (sudden and severe)
- E: eye problems (blurred vision, partial/full loss of vision)
- S: sudden leg pain
- ACHES are potential signs of blood clots, and require emergent medical attention

Taking COCs

Key reminders for use

Hormone Free Interval

- The hormone free interval (HFI) refers to when patients take placebo pills, resulting in **withdrawal bleeding**
- Shorter HFI = lower risk of ovulation = lower risk of pregnancy
- The HFI should **never exceed 7 days**
  - An HFI > 7 days increases risk of pregnancy, and a backup method should be used for 7 days upon the resumption of COC

Continuous Dosing

- Consecutive administration of active pills

Advantages	Disadvantages
• Decrease side effects that normally occur during HFI • Decrease anemia • Patient preference • Convenience • Increase adherence	• Lacking long-term safety data • Delay in recognition of pregnancy • Increase cost (but reduces cost of feminine hygiene products)

Formulations

Monophasic

- Same hormone doses for entire 21-day cycle

Multiphasic

- Hormone doses (P or E or both) vary during the active pill phase
- No clinical advantage compared to monophasic

Extended Cycle Formulations

- 84/7
- Active pills for 3 consecutive months so patient experiences withdrawal bleeding every 3 months instead of every month
- Same concept can be achieved with 21/7 packs by taking consecutively for 3 months

Efficacy of COCs

Perfect use	Typical use
>99%	~91%

Selecting an Initial COC

Consider the following patient-specific factors to help guide initial COC selection

COC Comparison Chart

COC	Estrogen (mcg)	Progestin	Estrogen Activity	Progestin Activity	Androgen Activity	Multi-Phasic
LoLo	Ultra-low (10)	1st gen	+	+++	+++	
Minestrin/Loestrin	Low (20/30)	1st gen	+/++	+++	+++	
Brevicon 0.5/1	Low (35)	1st gen	+++	+/+++	+/+++	
Synphasic	Low (35)	1st gen	+++	++	++	Yes (Bi)
Alesse/Aviane/ Alysena	Low (20)	2nd	+	+	++	
Ovral/Portia/Ovima	Low (30)	2nd	++	++	+++	
Triquilar	30-40-30	2nd	++	+	++	Yes (Tri)
Marvelon/Apri/Freya/ Mirvala	Low (30)	3rd	++	+++	+	
Linessa	Low (25)	3rd	++	+++	+	Yes (Tri)
Tri-Cira/Tri-Jordyna/Tricira-Lo	Low (35/35/25)	3rd	+++	+	+	Yes (Tri)
Yasmin/Zamine	Low (30)	4th	++	++	-------	
Yaz/Mya	Low (20)	4th	+	++	-------	

Considering COC Initiation

Absolute Contraindications

- Age ≥35 years and smoking ≥15 cigarettes per day
- Hypertension (systolic ≥160 mmHg or diastolic ≥100 mmHg)
- VTE
- Current breast cancer
- Migraine with aura
- Severe (decompensated) cirrhosis
- History of stroke of heart disease

Considerations

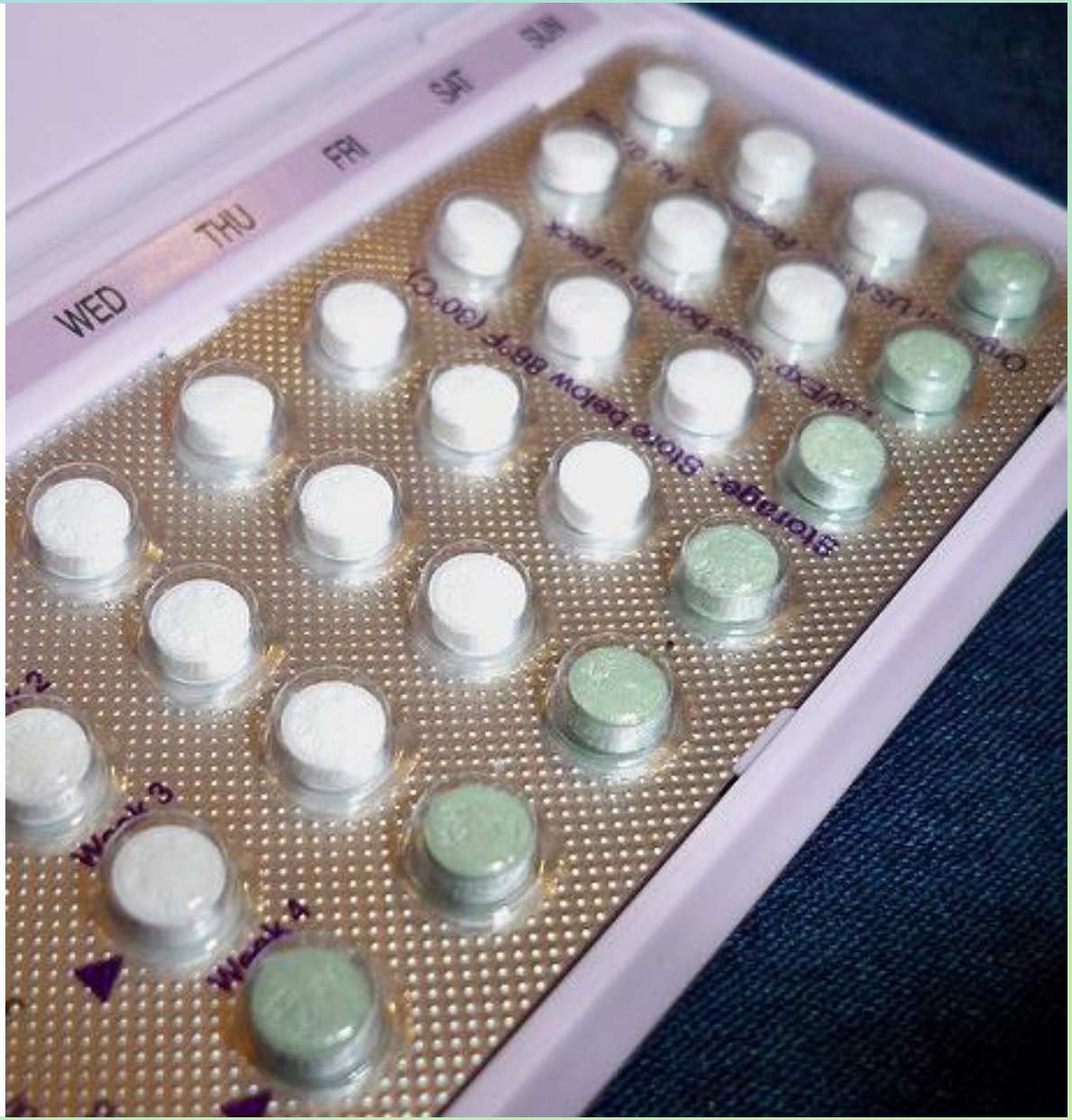
- Age ≥35 years and smoking <15 cigarettes per day
- Hypertension (systolic 140 to 159 mmHg or diastolic 90 to 99 mmHg)
- Past breast cancer with NED x 5 years
- Current gallbladder disease
- Superficial venous thrombosis

Acne

- All COCs are beneficial in acne
- The following are officially indicated for acne
  - Tri-cyclen
  - Alesse
  - Yaz
  - Yasmin

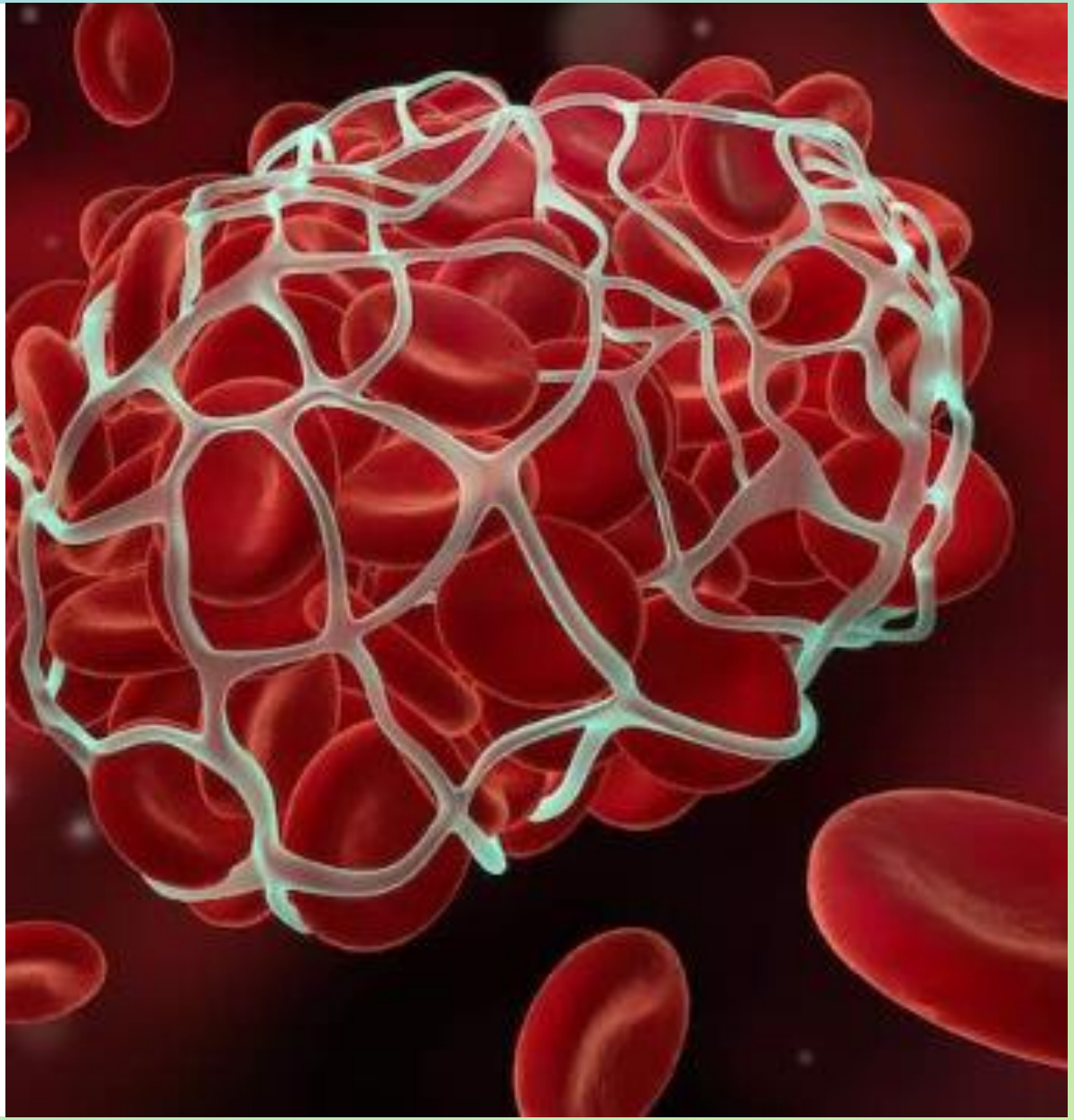
Obesity

- The majority of studies do not show that obesity results in decreased oral contraceptive efficacy
- However, it may be possible that there is slightly increased failure with COCs in patients with a BMI >30



Venous Thromboembolism

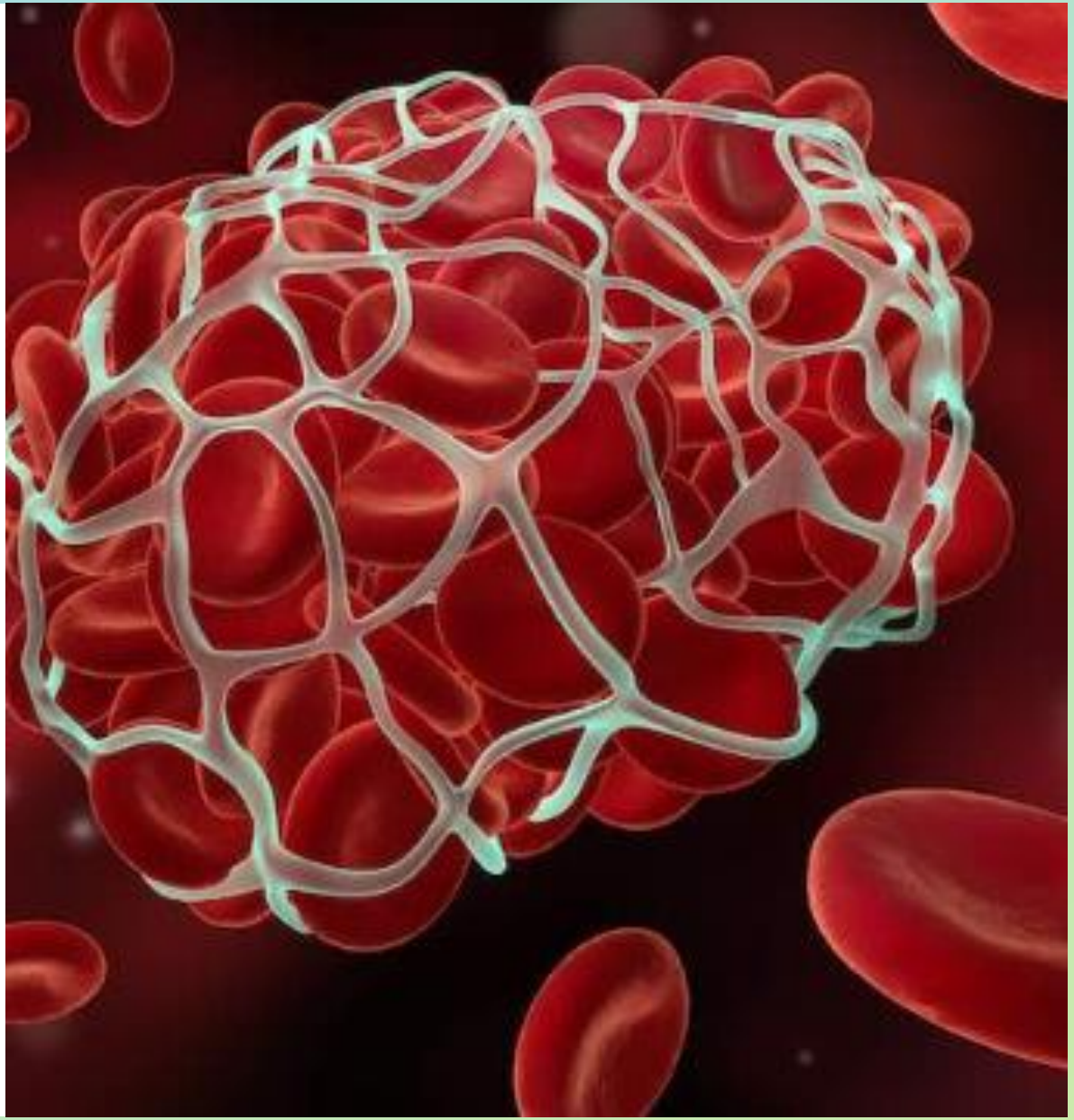
- COCs are associated with an increased risk of VTEs (2-3x ↑)
  - No significant difference in risk between different COCs
- NNH = 2,500/year as most patients have a **low baseline risk**
- This risk comes from the **estrogen*** component



Venous Thromboembolism: Additional Risk Factors

- BMI ≥ 30 kg/m2
- Age ≥ 35 years
- Previous VTE
- Smoking
- Immobility

Having the following risk factors can increase the patients baseline risk of VTE with COCs



Post-Partum

- Why can't COCs be started immediately after delivery?
  - After delivery, patients stay in a **hypercoagulable state** for weeks, and are therefore at an increased risk for VTE
  - May decrease breast milk production in those who are choosing to breastfeed so need to allow time for breastfeeding to be established

Initiating COCs Post-Partum (PP)

- Not breastfeeding: 3 weeks PP
- Breastfeeding: 6 weeks PP

COCs should never be started less than 21 days Post-Partum

Migraine

- Migraine **with** aura
  - Contraindicated
  - Estrogen may increase risk of stroke
- Migraine **without** aura
  - + no other risk factors for stroke: may use COC
  - Triggered by menses: consider continuous dosing

Anxiety/ Depression

- COCs may worsen depression, or increase one's risk of developing depression
- Depression is a symptom of excess progestin

Consider starting a COC with lower progestin activity

Adherence Issues

- Consider continuous dosing
  - Consistency in routine may help to increase adherence
  - Less likely to have HFI exceed 7 days
- For patients with cost-concerns, select cheaper COCs
  - Generic is cheaper than brand name
  - Monophasic cheaper than multiphasic

Brand vs Generic

- For a generic medication to be approved, it must demonstrate equivalency to the brand name
- Generic and brand name will contain the same active ingredients at the same doses, but the inactive ingredients (fillers) may differ
- Generic = cheaper

Troubleshooting COCs

How to manage common challenges with COCs such as side effects and product discontinuations

Signs of Hormone Deficiency

Estrogen Deficiency

- Early bleeding: days 1-9
- Atrophic vaginitis
- Vasomotor symptoms (hot flashes, night sweats, etc.)
- Continuous spotting
- Absence of withdrawal bleeding
- Management: Higher estrogen content (30-35mcg)

Progestin Deficiency

- Late bleeding: days 10-21
- Delayed withdrawal bleeding
- Management: Higher progestin content, monophasic product

Signs of Hormone Excess

Estrogen

- Increased menstrual bleeding
- Increased breast size
- Vascular headaches
- Dysmenorrhea
- Hypertension
- Thromboembolism
- Management: Lower estrogen (10-20mcg)

Progestin

- Depression
- Breast tenderness
- Decreased libido
- Weight gain/increased appetite
- Yeast infection
- Fatigue
- Management: Lower progestin

Other Hormonal Abnormalities

Excess Estrogen +/- Progestin Deficiency

- Nausea/Vomiting
- Headache
- Weight Gain
- Bloating
- Dizziness
- Leg Cramps
- Management: Lower estrogen (10-20mcg), higher progestin, monophasic product

Excess Androgen

- Oily skin
- Increased libido
- Hirsutism
- Acne
- Management: Lower androgenic activity (3rd-4th generation progestin)

Addressing Hormonal Abnormalities

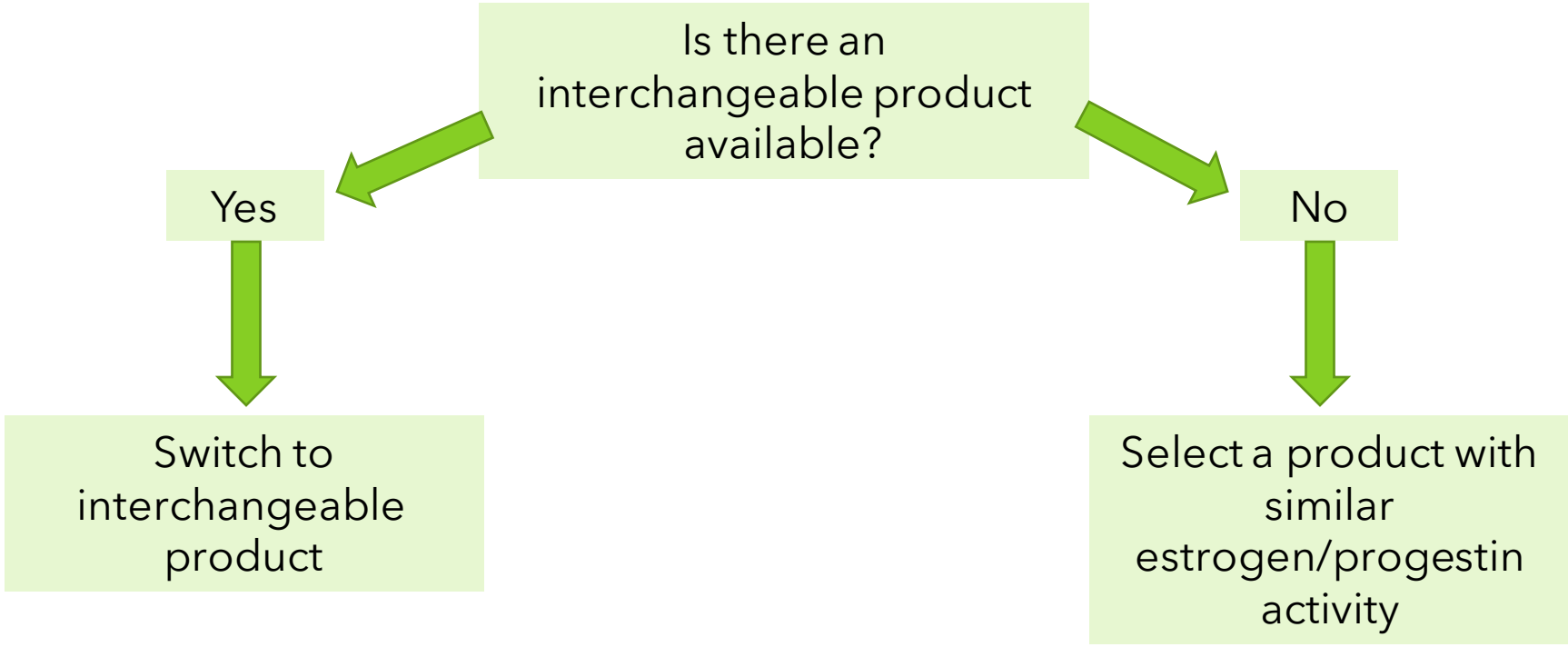
- Trial birth control for 3-6 months to see if side effects will resolve on their own
- If not resolved, switch to an alternative birth control that will address the hormonal abnormality causing the side effect(s)

Addressing Hormonal Abnormalities: Example

- Patient has been taking Synphasic for 8 months, and are still consistently experiencing increased menstrual bleeding and bloating
- These are signs of **estrogen excess**
- Switch to a birth control with similar progestin activity, and lower estrogen activity

Synphasic	Low (35)	1st gen	+++	++	++	Yes (Bi)
SWITCH TO						
Yaz/Mya	Low (20)	4th	+	++	-------	

What to do if your patient's COC is discontinued



Unsure of interchangeability? Check the interchangeability formulary!

COC	Estrogen (mcg)	Progestin	Estrogen Activity	Progestin Activity	Androgen Activity	Multi-Phasic
LoLo	Ultra-low (10)	1st gen	+	+++	+++	
Minestrin/Loestrin	Low (20/30)	1st gen	+/++	+++	+++	
Brevicon 0.5/1	Low (35)	1st gen	+++	+/+++	+/+++	
Synphasic	Low (35)	1st gen	+++	++	++	Yes (Bi)
Alesse/Aviane/ Alysena	Low (20)	2nd	+	+	++	
Ovral/Portia/Ovima				++	+++	
Triquilar				+	++	Yes (Tri)
Marvelon/Apri/Freya/ Mirvala				+++	+	
Linessa	Low (25)	3rd	++	+++	+	Yes (Tri)
Tri-Cira/Tri-Jordyna/Tricira-Lo	Low (35/35/25)	3rd	+++	+	+	Yes (Tri)
Yasmin/Zamine	Low (30)	4th	++	++	-------	
Yaz/Mya	Low (20)	4th	+	++	-------	

Is there an interchangeable product available? Example: Alesse is discontinued. We can replace that product with Aviane or Alysena as they have the same hormones at the same doses as Alesse

Interchangeability

	ETHINYL ESTRADIOL/LEVONORGESTREL — 0.02 mg/0.1 mg — Tablets (21) ETHINYL ESTRADIOL/LEVONORGESTREL — 0,02 mg/0,1 mg — comprimés		Per Tablet	Par comprimé	Per Tablet	Par comprimé
02236974	Alesse	PFI	0.7471	0,7471	0.7845	0,7845
02387875	Alysena 21	APX	0.4638	0,4638	0.4870	0,4870
02298538	Aviane 21	TEV	0.4638	0,4638	0.4870	0,4870

Interchangeable products with Alesse, per Manitoba's interchangeability formulary
Link: https://residents.gov.mb.ca/forms.html?d=details&pub_id=10542&filter_keyword=interchangeability (select gray button furthest right)

FUN FACT: The interchangeability formulary also gives cost per tablet, for cost comparisons amongst products
Above, you can see that brand-name Alesse is more expensive than the generic equivalents

COC	Estrogen (mcg)	Progestin	Estrogen Activity	Progestin Activity	Androgen Activity	Multi-Phasic
LoLo	Ultra-low (10)	1st gen	+	+++	+++	
Minestrin/Loestrin	Low (20/30)	1st gen	+/++	+++	+++	
Brevicon 0.5/1	Low (35)	1st gen	+++	+/+++	+/+++	
		st gen	+++	++	++	Yes (Bi)
		2nd	+	+	++	
Ovral/Portia/Ovima	Low (30)	2nd	++	++	+++	
Triquilar	30-40-30	2nd	++	+	++	Yes (Tri)
Marvelon/Apri/Freya/ Mirvala	Low (30)					
Lin ssa	Low (25)	3rd	++	+++	+	Yes (Tri)
Tri-C a/Tri-Jordyna Tricira-Lo	Low (35/35/25)	3rd	+++	+	+	Yes (Tri)
Yasmin/Zamine	Low (30)	4th	++	++	-------	
Yaz/Mya	Low (20)	4th	+	++	-------	

What if Ovral was discontinued and all interchangeable products were on backorder?

Could consider switching to Yasmin/Zamine as they have similar hormonal activities

Emergency Contraception

Emergency Contraception

- Hormonal: emergency contraception pills (ECP)
  - LNG-EC
  - UPA-EC (ullipristal acetate)
  - Yuzpe method
    - two doses 12h apart
    - Less effective, more side effects (n/v)
- Post coital insertion of Cu-IUD
  - Most effective option
  - Up to 7d after UPI, though studies exist up to 10d

Table 5 Combined oral contraceptive pills for use as EC

	Pills per dose	Ethinyl estradiol (mcg/dose)	Levonorgestrel (mcg/dose)
Alesse	5	100	500
Triquilar	4 yellow	120	500
Min-Ovral	4	120	600

Factors affecting effectiveness of EC pills

- BMI
  - >30 decreased effectiveness of LNG-EC (2 x RCT, WHO data contradicted this)
  - No similar decrease found with UPA-EC
  - No recommendations for increased dosing
- Recommendation:
  - Offer UPA-EC or Cu IUD if BMI >30 as preferred options
  - LNG-EC next best option
  - Counsel about pregnancy risks if subsequent coitus

Cu-IUD for emergency contraception

Cu-IUD 380 mm^2 as EC

- Sterile inflammatory reaction in uterine cavity
- Cu ions and by products of inflammation
  - toxic to sperm and eggs
  - Increase fallopian smooth muscle activity
  - Stimulate myometrial contractility
- Inhibits implantation

Contraindications to EC

- Pills:
  - No absolute, except pregnancy (won't harm pregnancy but won't work) and hypersensitivity
- Cu-IUD
  - Same as for use for contraception
    - Ensure no pre-existing pregnancy prior to insertion
    - Don't insert if current or recent pelvic infection or current purulent cervicitis

Risks and side effects to EC

- Pills:
  - No specific risks
  - Side effects:
    - Nausea, vomiting, dizziness, fatigue
    - Next menses may be early, on time, or late
- Cu-IUD
  - Same as when used for contraception:
    - Risks: uterine perforation, infection, expulsion, if a pregnancy occurs it is more likely to be tubal
    - Side effects: discomfort or pain with insertion, increase in menstrual flow, spotting, and cramping

Emergency Contraception Summary

- Use ASAP after unprotected intercourse
  - Pills most effective first 72 hours (3 days), can be used up to 120 hours (5 days)
  - Cu-IUD up to 7 (or maybe 10) days as long as negative urine pregnancy test
- Cu-IUD is most effective option
- If BMI >=30 preference for UPA-EC or Cu-IUD then LNG-EC
- Ask about contraception needs going forward
  - Can use quick start method of COC or IM contraception day of or after LNG-EC
  - Wait 5d after UPA-EC to start COC or IM contraception
- Pregnancy test if no normal menstrual bleeding by 21d post EC
  - 28d if COC initiated and no withdrawal bleeding
  - If using IM contraception or continuous hormone contraception recommend day 21 urine pregnancy test

Thank you for your time and attention

- Alora Simpson simpso39@myumanitoba.ca
- Marina Rountree-James mrountreejames@wrha.mb.ca

Progestin Only Contraceptives

Needles, implants, IUS and pills

Progestin-Only Contraception

- Most common side effect is bleeding changes.
- Does not appear to increase risk of VTE, MI, or stroke
- Early weight gain predictive of continued weight gain
- Efficacy not reduced if BMI >30
- IM associated with decrease in bone mineral density
  - vitamin D, calcium, weight-bearing exercise, decrease EtOH/ caffeine/ tobacco use)
- No demonstrated reduction in breast milk production
- Decreased risk of endometrial and ovarian cancer